DESCRIPTION

INDOLE COMPOUND AND MEDICINAL USE THEREOF

Technical Field

The present invention relates to a novel indole compound having an HLGPa (Human Liver Glycogen Phosphorylase a) inhibitory activity and use thereof as a pharmaceutical agent. More particularly, the present invention relates to a therapeutic agent for diabetes, which comprises an indole compound, a pharmaceutically acceptable salt thereof or a hydrate thereof.

Background Art

Diabetes is a chronic disease caused by abnormal metabolism of sugar, lipid and amino acid due to shortage of insulin action. When maintained without treatment, it shows hyperglycemia and urine sugar. Diabetes is divided into insulin-dependent type and non-insulin-dependent type, and about 90% of diabetic patients suffer from non-insulin-dependent diabetes mellitus.

In insulin dependent diabetes, since insulin secretory capacity has disappeared, ketonemia and acidosis easily occur, and when left as is, diabetic coma follows. Food restriction and oral hypoglycemic agent provide no therapeutic effect but only insulin does.

On the other hand, non-insulin-dependent diabetes mellitus (NIDDM) shows an insulin action lower than normal, but shows little propensity toward ketonemia and acidosis, and its treatment does not always require insulin.

Hypoglycemic agents currently in use for correcting hyperglycemia include insulin preparations, sulfonylurea agents (e.g., glibenclamide, torbutamide), biguanides (e.g., metformin), insulin sensitizers (e.g., troglitazone) and α-glucosidase inhibitors (e.g., acarbose).

Insulin preparations are pharmaceutical agents used for insulin dependent diabetes, which certainly decrease blood glucose but require administration by injection and are associated with the risk of causing hypoglycemia.

Sulfonylurea agents stimulate beta cell of pancreas and accelerate endogenous insulin secretion. However, the timing and amount of insulin secretion have nothing to do with blood glucose level, and vary depending on the timing and dose of drug administration. As side effects, therefore, hypoglycemia due to the duration of action of pharmaceutical agent often occurs. In addition, symptoms in digestive organs such as anorexia and the like are developed. They are prohibited to patients with severe ketosis or liver or renal dysfunction.

Biguanides are free of stimulation of beta cell of pancreas, their single administration does not cause hypoglycemia in healthy individuals and diabetes patients. Predictable action mechanism includes increase in the use of sugar due to anaerobic glycolysis action, suppression of gluconeogenesis, suppression of absorption of sugar from intestinal tract and the like. As a side effect, they easily develop comparatively severe lactic acidic acidosis.

As insulin sensitizers, thiazolidine derivatives can be mentioned. The thiazolidine derivatives do not have an insulin secretion promoting action, enhance insulin action, and show an insulin receptor kinase activation, peripheral tissue glucose uptake promoting action, improvement of liver glucose production promotion and the like. As side effects, symptoms of digestive organs, edema and the like are developed, and decrease of red count, hematocrit and hemoglobin as well as increase in LDH are known to occur.

While α-glucosidase inhibitors delay digestion and absorption of carbohydrate from the gastrointestinal tract and suppress postprandial elevation of glycemia, they pose

problems of side effects such as abdominal distension, borborygmus, diarrhea and the like (JOSLIN'S DIABETES MELLITUS 13Th Edition 521-522).

As mentioned above, the use of these pharmaceutical agents is limited due to the presence of side effects and ineffective patients, and a hypoglycemic agent based on a new action mechanism has been desired.

It has been reported in recent years that NIDDM patients show increased amounts of glucose released from the liver during fasting as compared to healthy individuals. This sugar release from the liver suggests possibility as a treatment target of pharmaceutical agent for NIDDM.

The supply source of sugar in sugar release from the liver is glucose produced by gluconeogenesis and glycogenolysis. It has been reported that, in diabetic patients, the glycogenolysis is deeply involved in the glucose release from the liver, and glycogenolysis rate increases by 75% during fasted state as compared to healthy individuals. In NIDDM patients, glucose release from the liver transitionally increases after glucose loading, and involvement of glycogenolysis in this increase has been suggested. In type IV glycogenosis (liver glycogen phosphorylase deficiency), moreover, it is known that hypoglycemia is developed during fasted state.

These reports suggest that glycogenolysis plays a major role in glucose release from the liver.

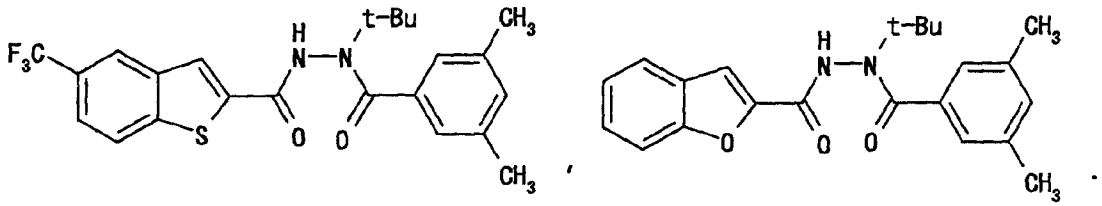
It is known that the glycogen decomposition is catalyzed by HLGPa, and glucose 1-phosphoric acid (G1-P) and glycogen (glucose units in the number of n-1) are produced by the glycogenolysis (glucose units in the number of n) by superphosphoric acid.

Therefore, a therapeutic agent for diabetes having an HLGPa inhibitory action deeply involved in this glycogen

decomposition, which is based on a new mechanism has been developed. As the situation stands, however, no agent having satisfactory activity has been found.

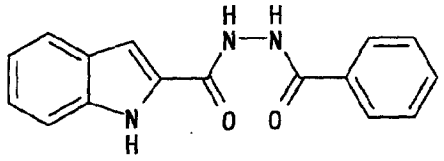
Incidentally, as compounds having a similar structure as that of the present invention, the following compounds are known.

For example, JP-A-5-39253 discloses the following compounds useful as harmful animal repellents:



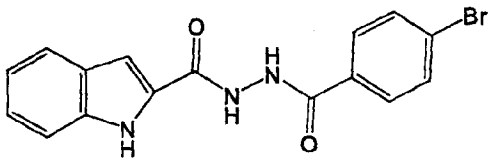
In this publication, no indole compound as in the present application is disclosed and use thereof is also completely different.

Tetrahedron Letter, vol. 23, pp. 2333-2335 (1972) discloses the following indole compound:



However, this reference does not disclose at all that an indole compound as in the present application has an HLGPa inhibitory activity and that the compound is effective as a therapeutic agent for diabetes.

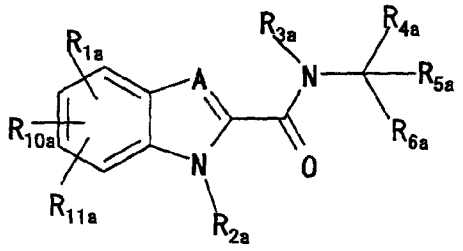
Yaoxue Xuebao, 19(10), 737-741 (1984) discloses



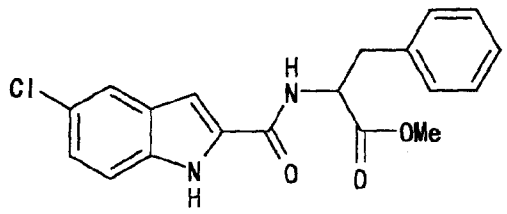
However, this reference does not disclose at all that an indole compound as in the present application has an HLGPa inhibitory activity and that the compound is effective as a

therapeutic agent for diabetes.

In addition, WO96/39384 (JP-T-10-511687) discloses, as a compound having an indole structure and a glycogen phosphorylase suppressive activity similar to the action of the present invention, the following formula:



wherein R_{4a} is a phenylalkyl group etc., R_{5a} is a hydrogen atom etc., R_{6a} is an alkoxycarbonyl group etc., R_{2a} is a hydrogen atom, R_{1a}, R_{10a} and R_{11a} are each independently a hydrogen atom, a halogen atom etc., R_{3a} is a hydrogen atom etc. and A is -N= etc. As a specific example, the following compound has been disclosed:



However, the compound of our invention is characterized in that it has an indole ring and a hydrazine and that the hydrazine is further bonded to a ring, but this compound does not essentially require a hydrazide structure.

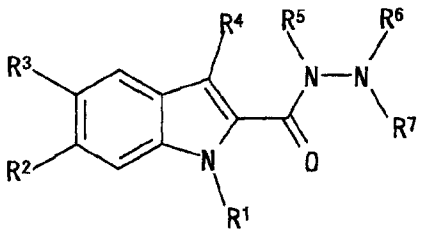
While the development of a therapeutic agent for diabetes, which is based on inhibition of HLGPa is currently ongoing, a therapeutic agent having satisfactory activity has not been found as yet. Accordingly, there is a strong demand for the development of a superior HLGPa inhibitor having a stronger activity and free of side effects as compared to conventional therapeutic agents for diabetes.

Disclosure of the Invention

In view of the above-mentioned problems, the present inventors have conducted intensive studies in an attempt to provide a therapeutic agent for diabetes having a useful HLGPa inhibitory activity and found that an indole compound represented by the following formula (1) has a stronger and remarkable HLGPa inhibitory activity as compared to conventional therapeutic agents for diabetes, which resulted in the completion of the present invention.

Accordingly, the present invention provides the following.

1. An indole compound represented by the formula (1)



(1)

wherein

R^1 is a hydrogen atom, a C_{1-6} alkyl group or an acyl group;

R^2 is a hydrogen atom or a halogen atom;

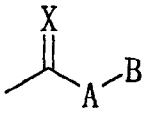
R^3 is a halogen atom, a C_{1-6} alkyl group, a C_{1-6} alkoxy group, a nitro group, an amino group, a hydroxyl group, a cyano group, an acyl group, an aralkyloxy group or a thiazolyl group wherein the thiazolyl group is optionally substituted by a C_{1-6} alkyl group or an amino group;

R^4 is a hydrogen atom or a C_{1-6} alkyl group;

R^5 is a hydrogen atom, a C_{1-6} alkyl group or a C_{2-7}-alkoxycarbonyl group;

R^6 is a hydrogen atom, a C_{1-6} alkyl group or an aralkyl group wherein the aralkyl group is optionally substituted by a halogen atom;

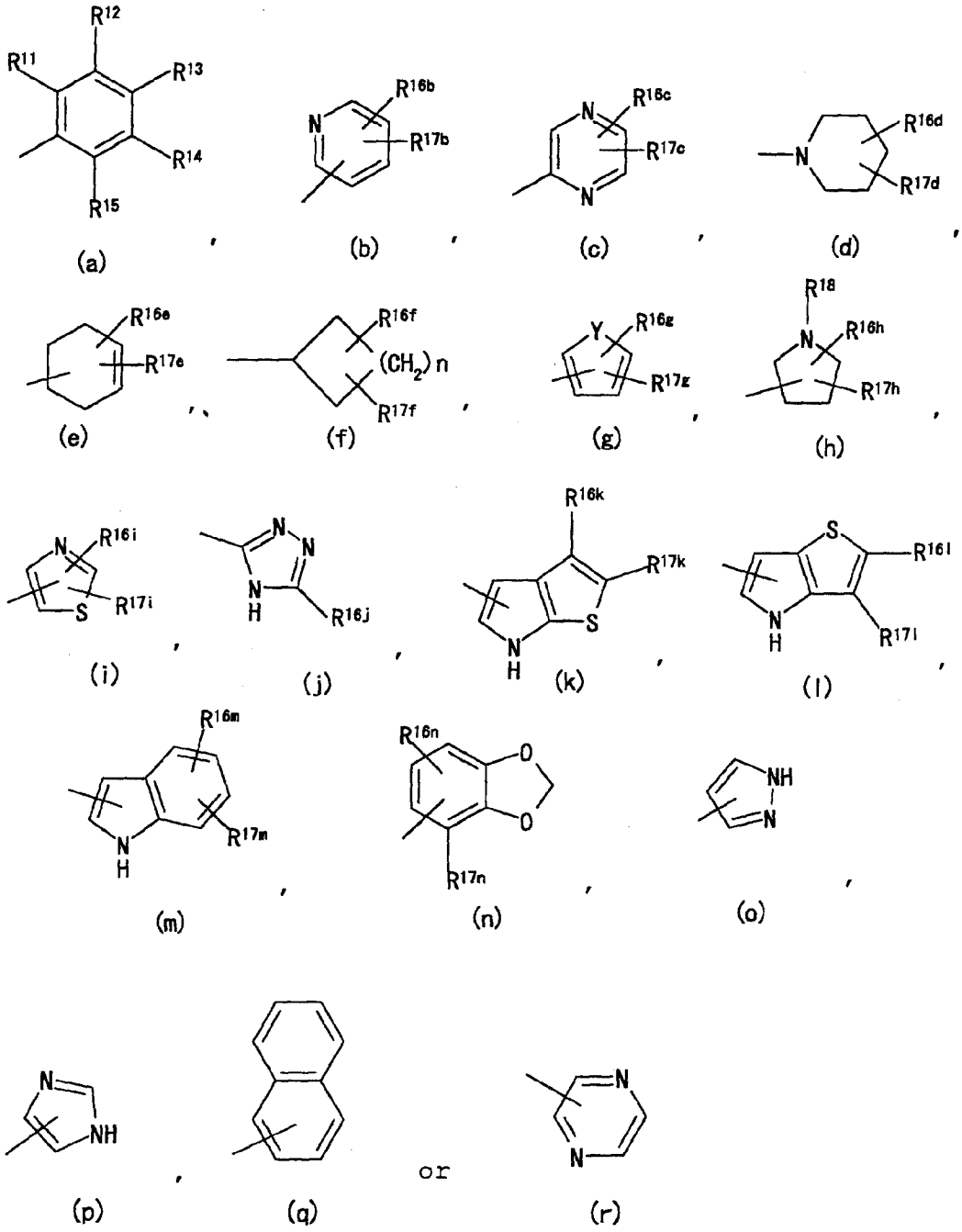
R^7 is



wherein X is =O, =S or =NH;

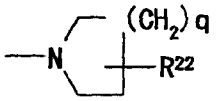
A is $-N(R^8)-$ wherein R^8 is a hydrogen atom, a C_{1-6} alkyl group or an aryl group optionally having substituents, $-C(R^9)(R^{10})-$ wherein R^9 and R^{10} are the same or different and each is independently a hydrogen atom, a hydroxyl group, an amino group, a C_{1-6} alkyl group, a C_{1-6} hydroxyalkyl group, a C_{2-7} alkoxycarbonylamino group or an acylamino group, or R^9 and R^{10} may form a C_{3-7} cycloalkyl group together with the adjacent carbon atom, $-(CH_2)_m-NH-$ wherein m is an integer of 1 to 4, -CO-, -S- or a single bond; and

B is

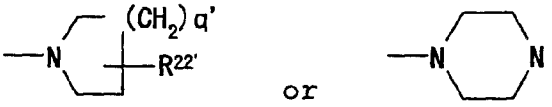


wherein R^{11}, R^{12}, R^{13}, R^{14} and R^{15} are the same or different and each is independently a hydrogen atom, a halogen atom, a C_{1-6} alkyl group, a C_{1-6} alkoxy group, a nitro group, a hydroxyl group, a cyano group, a haloalkyl group, an aralkyl group, an aryl group optionally having substituents, an aryloxy group, a tetrazolyl group, a triazolyl group, $-(CH_2)_p-CO-R^{19}$ wherein p is 0 or an integer of 1 to 4 and R^{19} is an aryl group optionally

having substituents, a hydroxyl group, a C_{1-6} alkoxy group or -$N(R^{20})(R^{21})$ wherein R^{20} and R^{21} are the same or different and each is independently a hydrogen atom, a C_{1-6} alkyl group, an aralkyl group or a C_{3-13} alkoxycarbonylalkyl group, or R^{20} and R^{21} may form, together with the adjacent nitrogen atom,



wherein q is an integer of 1 to 3 and R^{22} is a hydrogen atom, a hydroxyl group, a C_{1-6} alkoxy group, an amino group, a C_{2-12} dialkylamino group or a C_{2-7} alkoxycarbonylamino group, -O-$(CH_2)_r$-R^{23} wherein r is an integer of 1 to 4 and R^{23} is a hydroxyl group, an amino group, a C_{2-7} alkylcarbonyloxy group or -CO-R^{24} wherein R^{24} is a hydroxyl group, a C_{1-6} alkoxy group or -$N(R^{25})(R^{26})$ wherein R^{25} and R^{26} are the same or different and each is a hydrogen atom, a C_{1-6} alkyl group or an aralkyl group, or R^{25} and R^{26} may form, together with the adjacent nitrogen atom,



wherein q' and $R^{22'}$ are as defined for q and R^{22}, respectively, -O-CO-R^{27} wherein R^{27} is a C_{1-6} alkylamino group or a C_{2-12} dialkylamino group, or -$N(R^{28})(R^{29})$ wherein R^{28} and R^{29} are the same or different and each is a hydrogen atom, a C_{1-6} alkyl group, an aryl group optionally having substituents, an acyl group, -$(CH_2)_{p'}$-COO-R^{30} wherein p' is as defined for p and R^{30} is a hydrogen atom, an aryl group optionally having substituents or a C_{1-6} alkyl group wherein the C_{1-6} alkyl group is optionally substituted by a hydroxyl group, a trifluoromethyl group, an aryl group optionally having substituents, a morpholino group or a carboxyl group, -$CON(R^{31})(R^{32})$ wherein R^{31} and R^{32} are the same or different and each is a hydrogen atom, a C_{1-6} alkyl

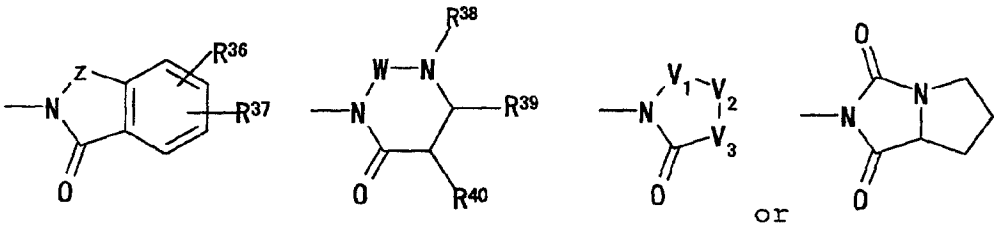
group or an aryl group optionally having substituents, $-CO-R^{33}$ wherein R^{33} is a C_{1-6} alkyl group or an aryl group optionally having substituents or $-CO-(CH_2)_{r'}-R^{34}$ wherein r' is as defined for r and R^{34} is a C_{1-6} alkylamino group, a C_{2-12} dialkylamino group, a C_{1-6} alkoxy group or a C_{2-7} alkylcarbonyloxy group, R^{16b}-R^{16n} and R^{17b}-R^{17n} are the same or different and each is a hydrogen atom, a halogen atom, a C_{1-6} alkyl group, an amino group, a hydroxyl group, a C_{1-6} alkoxy group or $-CON(R^{31'})(R^{32'})$ wherein $R^{31'}$ and $R^{32'}$ are as defined for R^{31} and R^{32},

R^{18} is a hydrogen atom or a C_{2-7} alkoxycarbonyl group,

Y is -S-, -O- or $-N(R^{35})-$ wherein R^{35} is a hydrogen atom or a C_{1-6} alkyl group, and

n is 0 or an integer of 1 to 4, or

R^6 and R^7 may form, together with the adjacent nitrogen atom,



(i) , (ii) , (iii) or (iv)

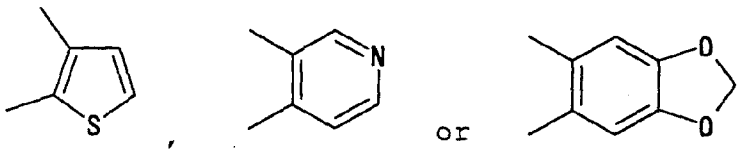
wherein R^{36} and R^{37} are the same or different and each is a hydrogen atom, a halogen atom, a C_{1-6} alkyl group, a C_{1-6} alkoxy group, an amino group, a nitro group, a hydroxyl group, a C_{2-7} alkoxycarbonyl group, a carboxyl group, a C_{2-7} haloalkylcarbonylamino group or $-O-CO-R^{41}$ wherein R^{41} is a C_{1-6} alkyl group, a C_{1-6} alkylamino group or a C_{2-12} dialkylamino group;

Z is $-CH_2-CH_2-$, $-C(R^{42})=CH-$, $-C(R^{42'})=N-$, -N=N-, -CO-, -CO-O-, $-CO-CH_2-O-$, $-CH_2-CO-NH-$, $-C(R^{42''})(R^{43})-N(R^{44})-$ wherein R^{42}, $R^{42'}$, $R^{42''}$ and R^{43} are the same or different and each is a hydrogen atom, a C_{1-6} alkyl group or an aryl group optionally having substituents and R^{44} is a hydrogen atom, a C_{2-7} alkoxycarbonyl group or a C_{1-6} alkyl group wherein the C_{1-6} alkyl group is

optionally substituted by a carboxyl group or a C_{2-7} alkoxycarbonyl group, or $-C(U)-N(R^{44'})-$ wherein U is =O or =S and $R^{44'}$ is as defined for R^{44} wherein an atom adjacent to the nitrogen atom on the fused ring in the formula (i) is described on the left end of each group;

R^{38} is a hydrogen atom, an aryl group optionally having substituents or a heteroaryl group;

R^{39} and R^{40} are the same or different and each is a hydrogen atom, a C_{1-6} alkyl group, a C_{1-6} alkoxy group or a C_{2-7} alkoxycarbonyl group, or R^{39} and R^{40} may form, together with the adjacent carbon atom,



or

W is $-CO-$, $-CS-$ or $-CH_2-$;

V_1 is $-CO-$, $-CS-$ or $-CH_2-$;

V_2 is $-O-$, $-CH_2-$ or $-N(R^{45})-$ wherein R^{45} is a hydrogen atom, a C_{1-6} alkyl group or an aryl group optionally having substituents; and

V_3 is $-CH(R^{46})-$ or $-N(R^{46'})-$ wherein R^{46} and $R^{46'}$ are each a hydrogen atom, an aralkyl group, a heteroaryl group or an aryl group optionally having substituents,

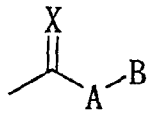
a pharmaceutically acceptable salt thereof or a prodrug thereof (hereinafter sometimes to be abbreviated as the compound (1) of the present invention.

2. The indole compound of 1 above,

wherein

R^6 is a hydrogen atom, a C_{1-6} alkyl group or an aralkyl group wherein the aralkyl group is optionally substituted by a halogen atom;

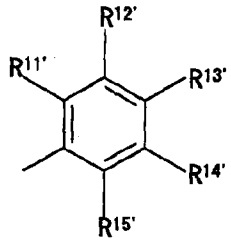
R^7 is



wherein X is =O, =S or =NH;

A is $-N(R^{8'})-$ wherein $R^{8'}$ is a hydrogen atom, a C_{1-6} alkyl group or a phenyl group optionally having substituents, $-C(R^{9'})(R^{10'})-$ wherein $R^{9'}$ and $R^{10'}$ are the same or different and each is a hydrogen atom, a hydroxyl group, an amino group, a C_{1-6} alkyl group, a C_{1-6} hydroxyalkyl group, a C_{2-7} alkoxycarbonylamino group or an acylamino group, or $R^{9'}$ and $R^{10'}$ may form, together with the adjacent carbon atom, a C_{3-7} cycloalkyl group, $-(CH_2)_m-$ NH- wherein m is an integer of 1 to 4, -CO-, -S- or a single bond; and

B is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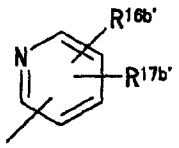
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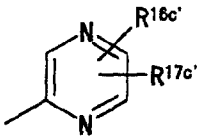
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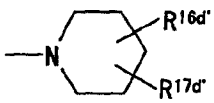
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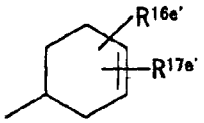
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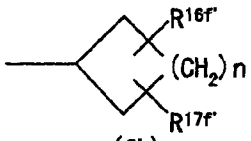
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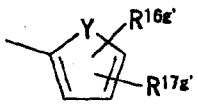
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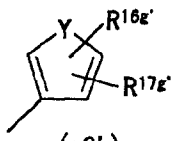
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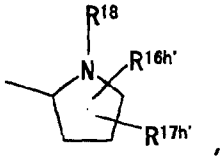
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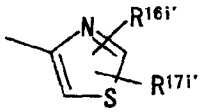
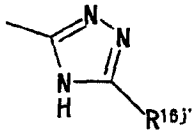

(i')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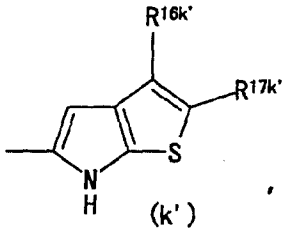
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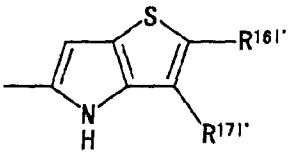
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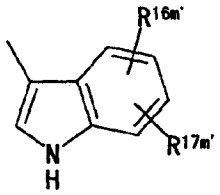
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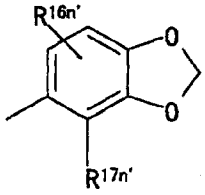
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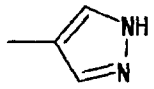
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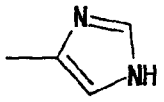
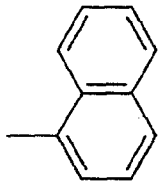
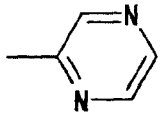

(p')


(q')

or


(r')

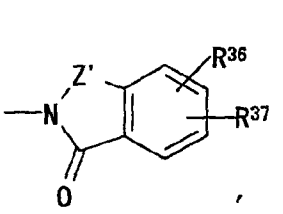
wherein $R^{11'}$, $R^{12'}$, $R^{13'}$, $R^{14'}$ and $R^{15'}$ are the same or different and each is a hydrogen atom, a halogen atom, a C_{1-6} alkyl group, a C_{1-6} alkoxy group, a nitro group, a hydroxyl group, a cyano group, a haloalkyl group, an aralkyl group, a phenyl group optionally having substituents, an aryloxy group, a tetrazolyl group, a triazolyl group, $-(CH_2)_p-CO-R^{19'}$ wherein p is 0 or an

integer of 1 to 4 and $R^{19'}$ is a phenyl group optionally having substituents, a hydroxyl group, a C_{1-6} alkoxy group or -$N(R^{20})(R^{21})$- wherein R^{20} and R^{21} are as defined in the above-mentioned 1, -O-$(CH_2)_r$-R^{23} wherein r and R^{23} are as defined in the above-mentioned 1, -O-CO-R^{27} wherein R^{27} is as defined in the above-mentioned 1, or -$N(R^{28'})(R^{29'})$ wherein $R^{28'}$ and $R^{29'}$ are the same or different and each is a hydrogen atom, a C_{1-6} alkyl group, a phenyl group optionally having substituents, an acyl group, -$(CH_2)_{p'}$-COO-$R^{30'}$ wherein p' is as defined in the above-mentioned 1 and $R^{30'}$ is a hydrogen atom, a phenyl group optionally having substituents or a C_{1-6} alkyl group wherein the C_{1-6} alkyl group is optionally substituted by a hydroxyl group, a trifluoromethyl group, a phenyl group optionally having substituents, a morpholino group or a carboxyl group, -$CON(R^{31''})(R^{32''})$ wherein $R^{31''}$ and $R^{32''}$ are the same or different and each is a hydrogen atom, a C_{1-6} alkyl group or a phenyl group optionally having substituents, -CO-$R^{33'}$ wherein $R^{33'}$ is a C_{1-6} alkyl group or a phenyl group optionally having substituents or -CO-$(CH_2)_{r'}$-R^{34} wherein r' and R^{34} are as defined in the above-mentioned 1,

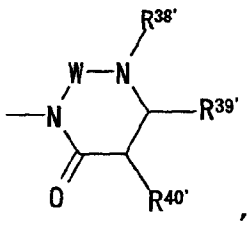
$R^{16b'}$-$R^{16n'}$ and $R^{17b'}$-$R^{17n'}$ are the same or different and each is a hydrogen atom, a halogen atom, a C_{1-6} alkyl group, an amino group, a hydroxyl group, a C_{1-6} alkoxy group or -$CON(R^{31'''})(R^{32'''})$ wherein $R^{31'''}$ and $R^{32'''}$ are as defined for $R^{31''}$ and $R^{32''}$, and

R^{18}, Y and n are as defined in the above-mentioned 1, or

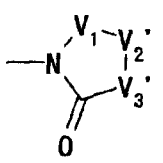
R^6 and R^7 may form, together with the adjacent nitrogen atom,



(i')

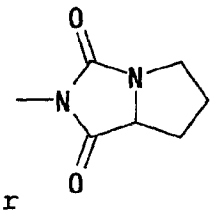


(ii')



(iii')

or



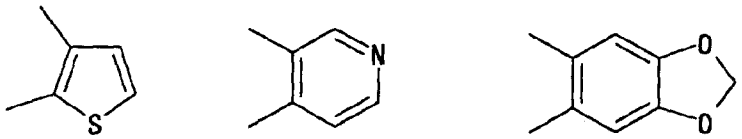
(iv)

wherein R^{36} and R^{37} are as defined in the above-mentioned 1;

Z' is $-CH_2-CH_2-$, $-C(R^{42})=CH-$, $-C(R^{42'})=N-$, $-N=N-$, $-CO-$, $-CO-O-$, $-CO-CH_2-O-$, $-CH_2-CO-NH-$, $-C(R^{42''})(R^{43})-N(R^{44})-$ wherein R^{42}, $R^{42'}$, $R^{42''}$ and R^{43} are the same or different and each is a hydrogen atom, a C_{1-6} alkyl group or a phenyl group optionally having substituents and R^{44} are as defined in the above-mentioned 1 or $-C(U)-N(R^{44'})-$ wherein U and $R^{44'}$ are as defined in the above-mentioned 1;

$R^{38'}$ is a hydrogen atom, a phenyl group optionally substituted by a halogen atom or a C_{1-6} alkyl group, or a pyridyl group;

$R^{39'}$ and $R^{40'}$ are both hydrogen atoms, or $R^{39'}$ and $R^{40'}$ may form, together with the adjacent carbon atom,



or

W and V_1 are as defined in the above-mentioned 1;

V_2' is $-O-$, $-CH_2-$ or $-N(R^{45})-$ wherein R^{45} is a hydrogen atom, a C_{1-6} alkyl group, a phenyl group optionally substituted by a halogen atom; and

V_3' is $-CH(R^{46})-$ or $-N(R^{46'})-$ wherein R^{46} and $R^{46'}$ are each a hydrogen atom, a benzyl group, a thienyl group, or a phenyl group optionally substituted by a halogen atom, a hydroxy group or a C_{1-6} alkoxy group,

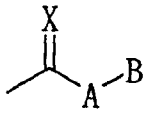
a pharmaceutically acceptable salt thereof or a prodrug thereof.

3. The indole compound of 1 above,

wherein

R^6 is a hydrogen atom, a C_{1-6} alkyl group or an aralkyl group wherein the aralkyl group is optionally substituted by a halogen atom;

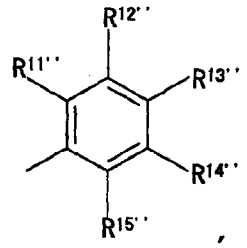
R^7 is

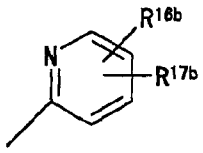


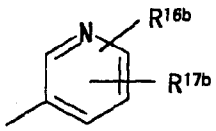
wherein X is as defined in the above-mentioned 1;

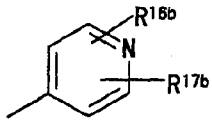
A is $-N(R^{8''})-$ wherein $R^{8''}$ is a hydrogen atom, a C_{1-6} alkyl group or an aryl group optionally having substituents, $-C(R^{9''})(R^{10''})-$ wherein $R^{9''}$ and $R^{10''}$ are the same or different and each is a hydrogen atom, a hydroxyl group, an amino group, a C_{1-6} alkyl group, a C_{1-6} hydroxyalkyl group or a C_{2-7} alkoxycarbonylamino group, or $R^{9''}$ and $R^{10''}$ may form, together with the adjacent carbon atom, a C_{3-7} cycloalkyl group, $-(CH_2)_m-NH-$ wherein m is as defined in the above-mentioned 1, -CO- or a single bond; and

B is


(a'')


(b1'')


(b2'')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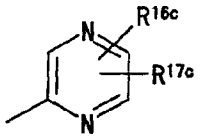
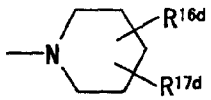
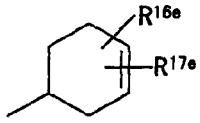
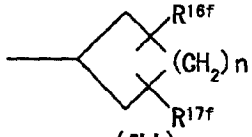
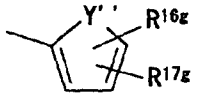
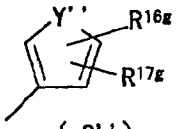

(c'')

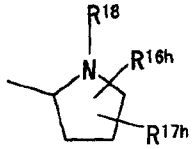

(d'')

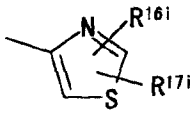

(e'')

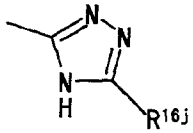

(f'')

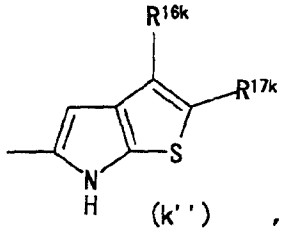

(g1'')

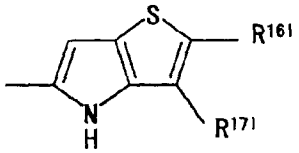

(g2'')

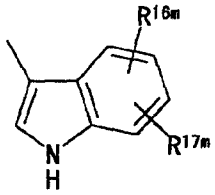

(h'')


(i'')

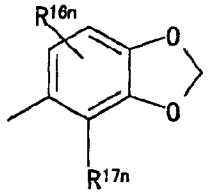

(j'')


(k'')


(l'')


(m'')

or


(n'')

wherein $R^{11''}$, $R^{12''}$, $R^{13''}$, $R^{14''}$ and $R^{15''}$ are the same or different and each is a hydrogen atom, a halogen atom, a C_{1-6} alkyl group, a C_{1-6} alkoxy group, a nitro group, a hydroxyl group, a cyano group, a haloalkyl group, an aralkyl group, an aryl group optionally having substituents, an aryloxy group, a

tetrazolyl group, a triazolyl group, $-(CH_2)_p-CO-R^{19}$ wherein p and R^{19} are as defined in the above-mentioned 1, $-O-(CH_2)_r-R^{23}$ wherein r and R^{23} are as defined in the above-mentioned 1, $-O-CO-R^{27}$ wherein R^{27} is as defined in the above-mentioned 1 or $-N(R^{28''})(R^{29''})$ wherein $R^{28''}$ and $R^{29''}$ are the same or different and each is a hydrogen atom, a C_{1-6} alkyl group, an aryl group optionally having substituents, $-(CH_2)_{p'}-COO-R^{30''}$ wherein p' is as defined for p and $R^{30''}$ is a hydrogen atom or a C_{1-6} alkyl group wherein the C_{1-6} alkyl group is optionally substituted by a hydroxyl group, a trifluoromethyl group or a carboxyl group, $-CON(R^{31})(R^{32})$ wherein R^{31} and R^{32} are as defined in the above-mentioned 1, $-CO-R^{33}$ wherein R^{33} is as defined in the above-mentioned 1 or $-CO-(CH_2)_{r'}-R^{34}$ wherein r' and R^{34} are as defined in the above-mentioned 1,

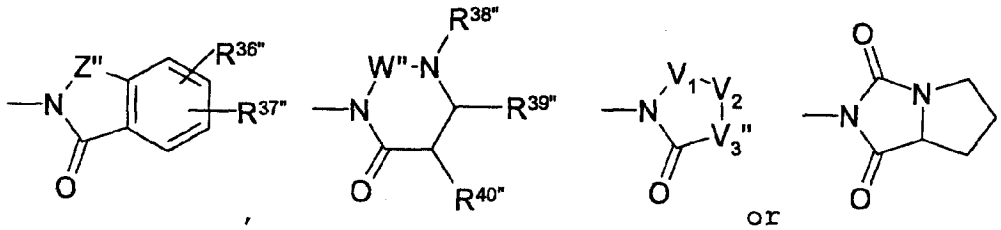
R^{16b}-R^{16n} and R^{17b}-R^{17n} are as defined in the above-mentioned 1,

R^{18} is as defined in the above-mentioned 1,

Y'' is -S- or $-N(R^{35})-$ wherein R^{35} is as defined in the above-mentioned 1, and

n is as defined in the above-mentioned 1, or

R^6 and R^7 may form, together with the adjacent nitrogen atom,



(i") (ii") (iii") (iv)

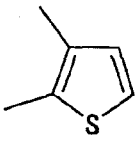
wherein $R^{36''}$ and $R^{37''}$ are the same or different and each is a hydrogen atom, a halogen atom, a C_{1-6} alkyl group, a C_{1-6} alkoxy group, an amino group, a hydroxyl group or $-O-CO-R^{41}$ wherein R^{41} are as defined in the above-mentioned 1;

Z'' is, $-CH_2-CH_2-$, $-C(R^{42})=CH-$, $-N=N-$, $-CO-$, $-CO-O-$, $-CO-CH_2-O-$, $-CH_2-CO-NH-$, $-C(R^{42''})(R^{43})-N(R^{44''})-$ wherein R^{42}, $R^{42''}$ and R^{43} are as defined in the above-mentioned 1 and $R^{44''}$ is a hydrogen atom,

a C_{1-6} alkyl group or a C_{2-7} alkoxycarbonyl group or -C(U)-N($R^{44'''}$)- wherein U is =O or =S and $R^{44'''}$ is as defined for $R^{44''}$;

$R^{38''}$ is a hydrogen atom or an aryl group optionally having substituents;

$R^{39''}$ and $R^{40''}$ are the same or different and each is a hydrogen atom, a C_{1-6} alkyl group or a C_{2-7} alkoxycarbonyl group, or $R^{39''}$ and $R^{40''}$ may form, together with the adjacent carbon atom,



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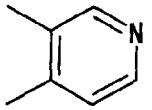

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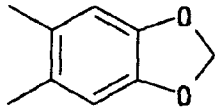


W'' is -CO- or $-CH_2-$;

V_1 and V_2 are as defined in the above-mentioned 1; and

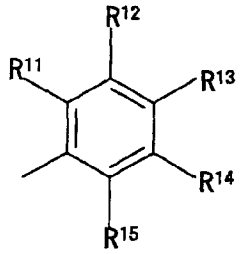
V_3'' is $-CH(R^{46''})-$ or $-N(R^{46'''})-$ wherein $R^{46''}$ and $R^{46'''}$ are the same or different and each is a hydrogen atom or an aryl group optionally having substituents,

a pharmaceutically acceptable salt thereof or a prodrug thereof.

4. The indole compound of 1 above, wherein R^1, R^2, R^4, R^5 and R^6 are each a hydrogen atom, a pharmaceutically acceptable salt thereof or a prodrug thereof.

5. The indole compound of 4 above, wherein R^3 is a halogen atom or a C_{1-6} alkyl group, a pharmaceutically acceptable salt thereof or a prodrug thereof.

6. The indole compound of 4 above, wherein X=O, A is a single bond and B is

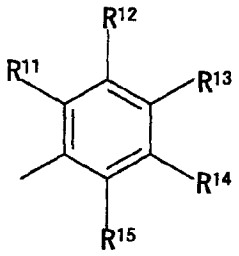


(a)

a pharmaceutically acceptable salt thereof or a prodrug

thereof.

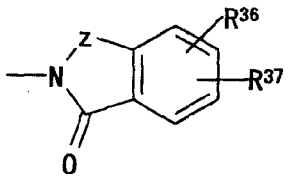
7. The indole compound of 4 above, wherein X=NH, A is a single bond and B is



(a)

a pharmaceutically acceptable salt thereof or a prodrug thereof.

8. The indole compound of 1 above, wherein R^6 and R^7 may form, together with the adjacent nitrogen atom,



(i)

a pharmaceutically acceptable salt thereof or a prodrug thereof.

9. The indole compound of 1 above, which is selected from the group consisting of

benzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2-aminobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2-hydroxybenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

3-(2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenylcarbamoyloxy)-2,2-dimethylpropionic acid,

benzoic acid 2-(5-chloro-1H-indole-2-carbonyl)-1-methylhydrazide,

benzoic acid 2-(1-acetyl-5-chloro-1H-indole-2-carbonyl)hydrazide,

5-chloro-1H-indole-2-carboxylic acid 2-(imino-phenyl-methyl)hydrazide,

5-aminothiazole-4-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

benzoic acid 2-(5-fluoro-1H-indole-2-carbonyl)hydrazide,

cyclohexanecarboxylic acid 2-(5-fluoro-1H-indole-2-carbonyl)hydrazide,

thiophene-2-carboxylic acid 2-(5-fluoro-1H-indole-2-carbonyl)hydrazide,

4-nitrobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2-methylbenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

4-methylbenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2-methoxybenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

3-methoxybenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

4-methoxybenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

3-methylbenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2-chlorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

3-chlorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

4-chlorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

4-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)benzoic acid methyl ester,

cyclohexanecarboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2,4-dichlorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2,6-dichlorobenzoic acid 2-(5-chloro-1H-indole-2-

carbonyl)hydrazide,

2,4-difluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

biphenyl-2-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

3-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

3-trifluoromethylbenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

4-trifluoromethylbenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2-trifluoromethylbenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

benzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide,

benzoic acid 2-(5-chloro-3-methyl-1H-indole-2-carbonyl)hydrazide,

benzoic acid 2-(5,7-dichloro-1H-indole-2-carbonyl)hydrazide,

2-aminobenzoic acid 2-(5-isopropyl-1H-indole-2-carbonyl)hydrazide,

2-amino-4-fluorobenzoic acid 2-(5-isopropyl-1H-indole-2-carbonyl)hydrazide,

2-aminobenzoic acid 2-(5-fluoro-1H-indole-2-carbonyl)hydrazide,

2-aminobenzoic acid 2-(6-chloro-1H-indole-2-carbonyl)hydrazide,

3-amino-4-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)benzoic acid methyl ester,

3-aminoisonicotinic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

isonicotinic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

nicotinic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

pyridine-2-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

3-(dimethylamino)benzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

N-(3-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenyl)acetamide,

N-(2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenyl)acetamide,

4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)-2-methylhydrazide,

2-(2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenoxy)acetic acid methyl ester,

2-(2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenoxy)acetic acid,

2-(dimethylamino)benzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenoxy-N,N-dimethylacetamide,

2-methylaminobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2-amino-4-chlorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2-amino-6-chlorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2-amino-3-chlorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2-amino-5-chlorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

4-cyanobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

4-(1H-tetrazol-5-yl)benzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

3-(1H-tetrazol-5-yl)benzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2-(2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)anilino)acetic acid,

2-aminobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide,
2-amino-4-fluorobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide,
methyl (2-(2-(5-methyl-1H-indole-2-carbonyl)hydrazinocarbonyl)phenyl)carbamate,
2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenyl dimethylcarbamate,
2-aminobenzoic acid 2-(5-ethyl-1H-indole-2-carbonyl)hydrazide,
2-amino-4,5-difluorobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide,
2-(2-hydroxyethoxy)benzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,
2-(3-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenoxy)acetic acid methyl ester,
2-(3-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenoxy)acetic acid,
2-(3-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenoxy)-N,N-dimethylacetamide,
2-methylthiazole-4-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,
4-(2H-[1,2,4]triazol-3-yl)benzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,
3-(2H-[1,2,4]triazol-3-yl)benzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,
1,3-dihydroxy-2-propyl (2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenyl)carbamate,
3-((2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenyl)carbamoyloxy)-2,2-dimethylpropionic acid,
thiophene-2-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,
furan-2-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2,6-dichloronicotinic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1H-pyrrole-2-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1H-imidazole-4-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

pyrazine-2-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

thiophene-3-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

furan-3-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

5-chlorothiophene-2-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

3-chlorothiophene-2-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-methyl-1H-pyrrole-2-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

5-methylthiophene-2-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

3-methylthiophene-2-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2,6-difluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2,3-difluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

5-chloro-1H-indole-2-carboxylic acid 2-(naphthalene-1-carbonyl)hydrazide,

3,4,5-trifluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2,3,4,5-tetrafluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2-amino-4-methylbenzoic acid 2-(5-chloro-1H-indole-2-

carbonyl)hydrazide,

2-amino-4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2-amino-5-methylbenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2-amino-6-methylbenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2-amino-3-methylbenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2-amino-4,5-difluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

3-aminothiophene-2-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2-aminobenzoic acid 2-(5-bromo-1H-indole-2-carbonyl)hydrazide,

2-amino-4-fluorobenzoic acid 2-(5-bromo-1H-indole-2-carbonyl)hydrazide,

1H-pyrazole-4-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

methyl (2-(2-(5-fluoro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenyl)carbamate,

1-methyl-1H-pyrrole-2-carboxylic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide,

thiophene-3-carboxylic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide,

4H-thieno[3,2-b]pyrrole-5-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

phenyl (2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenyl)carbamate,

benzyl (2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenyl)carbamate,

2-hydroxyethyl (2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenyl)carbamate,

3-hydroxypropyl (2-(2-(5-chloro-1H-indole-2-

carbonyl)hydrazinocarbonyl)phenyl)carbamate,
2-((2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenyl)carbamoyloxy)acetic acid,
2-((2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenyl)carbamoyloxymethyl)-2-methylmalonic acid,
methyl 2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenylcarbamate,
cyclohexanecarboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)-1-methylhydrazide,
thiophene-2-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)-1-methylhydrazide,
benzoic acid 2-(1H-indole-2-carbonyl)hydrazide,
benzoic acid 2-(5-chloro-1-methyl-1H-indole-2-carbonyl)hydrazide,
benzoic acid 2-(5-methoxy-1H-indole-2-carbonyl)hydrazide,
benzoic acid 2-(5-isopropyl-1H-indole-2-carbonyl)hydrazide,
benzoic acid 2-(5-nitro-1H-indole-2-carbonyl)hydrazide,
benzoic acid 2-(5-benzyloxy-1H-indole-2-carbonyl)hydrazide,
benzoic acid 2-(6-chloro-1H-indole-2-carbonyl)hydrazide,
6H-thieno[2,3-b]pyrrole-5-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,
5-chloro-1H-indole-2-carboxylic acid 2-((2-fluorophenyl)-imino-methyl)hydrazide,
5-chloro-1H-indole-2-carboxylic acid 2-((3-fluorophenyl)-imino-methyl)hydrazide,
5-chloro-1H-indole-2-carboxylic acid 2-((4-fluorophenyl)-imino-methyl)hydrazide,
5-chloro-1H-indole-2-carboxylic acid 2-(imino-(p-tolyl)-methyl)hydrazide,
5-chloro-1H-indole-2-carboxylic acid 2-((4-chlorophenyl)-imino-methyl)hydrazide,
5-chloro-1H-indole-2-carboxylic acid 2-((3-chlorophenyl)-

imino-methyl)hydrazide,

5-chloro-1H-indole-2-carboxylic acid 2-((3-fluorophenyl)-imino-methyl)hydrazide,

5-chloro-1H-indole-2-carboxylic acid 2-(imino-(o-tolyl)-methyl)hydrazide,

5-chloro-1H-indole-2-carboxylic acid 2-(imino-(m-tolyl)-methyl)hydrazide,

5-chloro-1H-indole-2-carboxylic acid 2-(imino-(thiophen-2-yl)-methyl)hydrazide,

5-chloro-1H-indole-2-carboxylic acid 2-(imino-(pyridin-2-yl)-methyl)hydrazide,

5-chloro-1H-indole-2-carboxylic acid 2-((furan-2-yl)-imino-methyl)hydrazide,

5-chloro-1H-indole-2-carboxylic acid 2-((2-chloro-6-fluorophenyl)-imino-methyl)hydrazide,

5-chloro-1H-indole-2-carboxylic acid 2-(imino-(2-trifluoromethylphenyl)-methyl)hydrazide,

5-chloro-1H-indole-2-carboxylic acid 2-(imino-(pyrazin-2-yl)-methyl)hydrazide,

3-aminobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

3-methoxybenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

5-amino-2-methylthiazole-4-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

5-chloro-1H-indole-2-carboxylic acid (1,2,3,4-tetrahydro-2,4-dioxoquinazolin-3-yl)amide,

5-chloro-1H-indole-2-carboxylic acid (2,3-dihydro-2,4-dioxo-4H-benzo[e][1,3]oxazin-3-yl)amide,

5-chloro-1H-indole-2-carboxylic acid (1,2,3,4-tetrahydro-4-oxo-2-thioxoquinazolin-3-yl)amide,

5-chloro-1H-indole-2-carboxylic acid (3,4-dihydro-2-methyl-4-oxoquinazolin-3-yl)amide,

5-chloro-1H-indole-2-carboxylic acid (3,4-dihydro-4-

oxoquinazolin-3-yl)amide,

5-chloro-1H-indole-2-carboxylic acid (1,2,3,4-tetrahydro-4-oxoquinazolin-3-yl)amide,

5-chloro-1H-indole-2-carboxylic acid (1,2,3,4-tetrahydro-2,5-dioxo-5H-benzo[e][1,4]diazepin-4-yl)amide,

5-chloro-1H-indole-2-carboxylic acid (2,3,4,5-tetrahydro-3,5-dioxo-benzo[f][1,4]oxazepin-4-yl)amide,

5-isopropyl-1H-indole-2-carboxylic acid (1,2,3,4-tetrahydro-2,4-dioxoquinazolin-3-yl)amide,

5-isopropyl-1H-indole-2-carboxylic acid (7-fluoro-1,2,3,4-tetrahydro-2,4-dioxoquinazolin-3-yl)amide,

5-fluoro-1H-indole-2-carboxylic acid (1,2,3,4-tetrahydro-2,4-dioxoquinazolin-3-yl)amide,

6-chloro-1H-indole-2-carboxylic acid (1,2,3,4-tetrahydro-2,4-dioxoquinazolin-3-yl)amide,

3-((5-chloro-1H-indole-2-carbonyl)amino)-1,2,3,4-tetrahydro-2,4-dioxoquinazoline-7-carboxylic acid methyl ester,

3-((5-chloro-1H-indole-2-carbonyl)amino)-1,2,3,4-tetrahydro-2,4-dioxoquinazoline-7-carboxylic acid,

5-chloro-1H-indole-2-carboxylic acid (1,2,3,4-tetrahydro-2,4-dioxo-6-(trifluoroacetylamino)quinazolin-3-yl)amide,

5-chloro-1H-indole-2-carboxylic acid (6-amino-1,2,3,4-tetrahydro-2,4-dioxoquinazolin-3-yl)amide,

5-chloro-1H-indole-2-carboxylic acid (5-chloro-1,2,3,4-tetrahydro-2,4-dioxoquinazolin-3-yl)amide,

5-chloro-1H-indole-2-carboxylic acid (6-chloro-1,2,3,4-tetrahydro-2,4-dioxoquinazolin-3-yl)amide,

5-chloro-1H-indole-2-carboxylic acid (7-chloro-1,2,3,4-tetrahydro-2,4-dioxoquinazolin-3-yl)amide,

5-chloro-1H-indole-2-carboxylic acid (8-chloro-1,2,3,4-tetrahydro-2,4-dioxoquinazolin-3-yl)amide,

2-(3-((5-chloro-1H-indole-2-carbonyl)amino)-1,2,3,4-tetrahydro-2,4-dioxoquinazolin-1-yl)acetic acid,

2-(3-((5-chloro-1H-indole-2-carbonyl)amino)-1,2,3,4-tetrahydro-2,4-dioxoquinazolin-1-yl)acetic acid methyl ester,
5-methyl-1H-indole-2-carboxylic acid (1,2,3,4-tetrahydro-2,4-dioxoquinazolin-3-yl)amide,
5-methyl-1H-indole-2-carboxylic acid (7-fluoro-1,2,3,4-tetrahydro-2,4-dioxoquinazolin-3-yl)amide,
5-ethyl-1H-indole-2-carboxylic acid (1,2,3,4-tetrahydro-2,4-dioxoquinazolin-3-yl)amide,
5-methyl-1H-indole-2-carboxylic acid (6,7-difluoro-1,2,3,4-tetrahydro-2,4-dioxoquinazolin-3-yl)amide,
5-methyl-1H-indole-2-carboxylic acid (1,2,3,4-tetrahydro-6-methoxy-2,4-dioxoquinazolin-3-yl)amide,
5-methyl-1H-indole-2-carboxylic acid (1,2,3,4-tetrahydro-6-hydroxy-2,4-dioxoquinazolin-3-yl)amide,
acetic acid 3-((5-methyl-1H-indole-2-carbonyl)amino)-1,2,3,4-tetrahydro-2,4-dioxoquinazolin-6-yl ester,
5-chloro-1H-indole-2-carboxylic acid (1,2,3,4-tetrahydro-2,4-dioxo-1-propylquinazolin-3-yl)amide,
5-chloro-1H-indole-2-carboxylic acid (1,2,3,4-tetrahydro-1-methyl-2,4-dioxoquinazolin-3-yl)amide,
N-(1,2,3,4-tetrahydro-7-nitro-2,4-dioxoquinazolin-3-yl)-5-chloro-1H-indole-2-carboxylic acid amide,
5-chloro-1H-indole-2-carboxylic acid (2,4-dioxoperhydropyrimidin-3-yl)amide,
5-chloro-1H-indole-2-carboxylic acid (4-oxo-2-thioxoperhydropyrimidin-3-yl)amide,
5-chloro-1H-indole-2-carboxylic acid (2,4-dioxo-1-phenylperhydropyrimidin-3-yl)amide,
5-chloro-1H-indole-2-carboxylic acid (4-oxo-1-phenylperhydropyrimidin-3-yl)amide,
5-chloro-1H-indole-2-carboxylic acid (1-(4-fluorophenyl)-2,4-dioxoperhydropyrimidin-3-yl)amide,
5-chloro-1H-indole-2-carboxylic acid (2,4-dioxo-1-(pyridin-2-

yl)perhydropyrimidin-3-yl)amide,

5-chloro-1H-indole-2-carboxylic acid (1-(3-fluorophenyl)-2,4-dioxoperhydropyrimidin-3-yl)amide,

5-chloro-1H-indole-2-carboxylic acid (1-(2-fluorophenyl)-2,4-dioxoperhydropyrimidin-3-yl)amide,

5-fluoro-1H-indole-2-carboxylic acid (2,4-dioxo-1-phenyl-perhydropyrimidin-3-yl)amide,

5-methyl-1H-indole-2-carboxylic acid (2,4-dioxo-1-phenyl-perhydropyrimidin-3-yl)amide,

5-chloro-1H-indole-2-carboxylic acid (1-(3-chlorophenyl)-2,4-dioxoperhydropyrimidin-3-yl)amide,

5-chloro-1H-indole-2-carboxylic acid (2,4-dioxo-1-(m-tolyl)perhydropyrimidin-3-yl)amide,

5-chloro-1H-indole-2-carboxylic acid (2,4-dioxo-1-(p-tolyl)perhydropyrimidin-3-yl)amide,

5-chloro-1H-indole-2-carboxylic acid (1-(4-chlorophenyl)-2,4-dioxoperhydropyrimidin-3-yl)amide,

5-chloro-1H-indole-2-carboxylic acid (2,4-dioxo-1-(o-tolyl)perhydropyrimidin-3-yl)amide,

5-chloro-1H-indole-2-carboxylic acid ((4S)-2,5-dioxo-4-phenylimidazolidin-1-yl)amide,

5-chloro-1H-indole-2-carboxylic acid (2,4-dioxo-1-phenylimidazolidin-3-yl)amide,

5-chloro-1H-indole-2-carboxylic acid (4-oxo-1-phenyl-2-thioxoimidazolidin-3-yl)amide,

5-chloro-1H-indole-2-carboxylic acid (4-oxo-1-phenylimidazolidin-3-yl)amide,

5-chloro-1H-indole-2-carboxylic acid (2-oxo-1-phenylimidazolidin-3-yl)amide,

5-chloro-1H-indole-2-carboxylic acid ((4R)-2,5-dioxo-4-phenylimidazolidin-1-yl)amide,

5-chloro-1H-indole-2-carboxylic acid ((4S)-1,3-dioxo-perhydropyrrolo[1,2-c]imidazol-2-yl)amide,

5-chloro-1H-indole-2-carboxylic acid ((4R)-1,3-dioxo-perhydropyrrolo[1,2-c]imidazol-2-yl)amide,

5-chloro-1H-indole-2-carboxylic acid ((4S)-4-benzyl-2,5-dioxoimidazolidin-1-yl)amide,

5-chloro-1H-indole-2-carboxylic acid ((4R)-4-benzyl-2,5-dioxoimidazolidin-1-yl)amide,

5-chloro-1H-indole-2-carboxylic acid (2,4-dioxoimidazolidin-3-yl)amide,

5-chloro-1H-indole-2-carboxylic acid (1-methyl-2,5-dioxo-4-phenylimidazolidin-1-yl)amide,

5-chloro-1H-indole-2-carboxylic acid (2,4-dioxo-1-(4-fluorophenyl)imidazolidin-3-yl)amide,

5-chloro-1H-indole-2-carboxylic acid (2,5-dioxo-4-(2-fluorophenyl)imidazolidin-1-yl)amide,

5-chloro-1H-indole-2-carboxylic acid (2,5-dioxo-4-(2-thienyl)imidazolidin-1-yl)amide,

5-chloro-1H-indole-2-carboxylic acid (2,5-dioxo-4-(4-fluorophenyl)imidazolidin-1-yl)amide,

5-chloro-1H-indole-2-carboxylic acid (2,5-dioxo-4-(4-chlorophenyl)imidazolidin-1-yl)amide,

5-chloro-1H-indole-2-carboxylic acid ((4S)-2,5-dioxo-4-(4-hydroxyphenyl)imidazolidin-1-yl)amide,

5-chloro-1H-indole-2-carboxylic acid ((4S)-2,5-dioxo-4-(4-methoxyphenyl)imidazolidin-1-yl)amide,

5-chloro-1H-indole-2-carboxylic acid ((4R)-2,5-dioxo-4-(4-methoxyphenyl)imidazolidin-1-yl)amide,

5-chloro-1H-indole-2-carboxylic acid 2-(anilinocarbonyl)hydrazide,

5-chloro-1H-indole-2-carboxylic acid 2-(phenylthiocarbonyl)hydrazide,

5-chloro-1H-indole-2-carboxylic acid 2-(2-phenylacetyl)hydrazide,

5-chloro-1H-indole-2-carboxylic acid 2-(2-oxo-2-

phenylacetyl)hydrazide,

5-chloro-1H-indole-2-carboxylic acid 2-((2-fluorophenyl)aminocarbonyl)hydrazide,

5-chloro-1H-indole-2-carboxylic acid 2-((3-fluorophenyl)aminocarbonyl)hydrazide,

5-chloro-1H-indole-2-carboxylic acid 2-((4-fluorophenyl)aminocarbonyl)hydrazide,

5-chloro-1H-indole-2-carboxylic acid 2-(anilinocarbonyl)-2-methylhydrazide,

5-chloro-1H-indole-2-carboxylic acid 2-((2-chloroanilino)carbonyl)hydrazide,

5-chloro-1H-indole-2-carboxylic acid 2-((3-chloroanilino)carbonyl)hydrazide,

5-chloro-1H-indole-2-carboxylic acid 2-((4-chloroanilino)carbonyl)hydrazide,

5-chloro-1H-indole-2-carboxylic acid 2-((1-phenylcyclopropane)carbonyl)hydrazide,

5-chloro-1H-indole-2-carboxylic acid 2-((1-phenylcyclopentane)carbonyl)hydrazide,

5-chloro-1H-indole-2-carboxylic acid 2-((1-phenylcyclohexane)carbonyl)hydrazide,

5-chloro-1H-indole-2-carboxylic acid 2-(2-phenylpropanoyl)hydrazide,

5-chloro-1H-indole-2-carboxylic acid 2-(3-hydroxy-2-phenylpropanoyl)hydrazide,

5-chloro-1H-indole-2-carboxylic acid 2-(2-methyl-2-phenylpropanoyl)hydrazide,

5-chloro-1H-indole-2-carboxylic acid 2-((2S)-2-amino-2-phenylacetyl)hydrazide,

N-(2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazino)-2-oxo-1-phenylethyl)acetamide,

2-morpholinoethyl (2-((2-(5-chloro-1H-indole-2-carbonyl)hydrazino)carbonyl)phenyl)carbamate p-

toluenesulfonate,

2-amino-4,5-difluorobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide benzenesulfonate,

2-amino-4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide benzenesulfonate,

3-(dimethylamino)benzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide methanesulfonate,

2-amino-4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide hydrochloride,

2-amino-4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide p-toluenesulfonate,

2-amino-4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide p-toluenesulfonate,

2-amino-4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide p-toluenesulfonate,

2-amino-4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide p-toluenesulfonate,

2-aminobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide p-toluenesulfonate,

2-aminobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide benzenesulfonate,

2-amino-4-fluorobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide benzenesulfonate,

3-aminobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide p-toluenesulfonate,

5-chloro-1H-indole-2-carboxylic acid 2-((2-chlorophenyl)-imino-methyl)hydrazide methanesulfonate,

5-chloro-1H-indole-2-carboxylic acid 2-((2-chlorophenyl)-imino-methyl)hydrazide p-toluenesulfonate,

5-chloro-1H-indole-2-carboxylic acid 2-((2-chlorophenyl)-imino-methyl)hydrazide hydrochloride,

5-chloro-1H-indole-2-carboxylic acid 2-(imino-phenyl-methyl)hydrazide methanesulfonate,

5-chloro-1H-indole-2-carboxylic acid 2-((2-chlorophenyl)-imino-methyl)hydrazide butenedioic acid salt,

5-chloro-1H-indole-2-carboxylic acid 2-((2-fluorophenyl)-imino-methyl)hydrazide hydrochloride,

5-chloro-1H-indole-2-carboxylic acid 2-((2-fluorophenyl)-imino-methyl)hydrazide methanesulfonate,

5-chloro-1H-indole-2-carboxylic acid 2-((1-imino-2-phenylethyl)hydrazide methanesulfonate,

5-chloro-1H-indole-2-carboxylic acid 2-((3-fluorophenyl)-imino-methyl)hydrazide hydrochloride,

5-chloro-1H-indole-2-carboxylic acid 2-((3,4-difluorophenyl)-imino-methyl)hydrazide methanesulfonate,

5-chloro-1H-indole-2-carboxylic acid 2-(imino-(2-methoxyphenyl)-methyl)hydrazide methanesulfonate,

5-chloro-1H-indole-2-carboxylic acid 2-((2,6-difluorophenyl)-imino-methyl)hydrazide methanesulfonate,

5-chloro-1H-indole-2-carboxylic acid 2-((2,4-difluorophenyl)-imino-methyl)hydrazide methanesulfonate,

5-chloro-1H-indole-2-carboxylic acid 2-((1,2-dimethyl-1H-pyrrol-5-yl)-imino-methyl)hydrazide methanesulfonate,

2-aminobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide p-toluenesulfonate,

2-aminobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide benzenesulfonate,

2-amino-4-fluorobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide benzenesulfonate,

2-(dimethylamino)benzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide p-toluenesulfonate,

2-amino-4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide methanesulfonate,

2-aminobenzoic acid 2-(5-bromo-1H-indole-2-carbonyl)hydrazide methanesulfonate,

2-amino-4-fluorobenzoic acid 2-(5-methyl-1H-indole-2-

carbonyl)hydrazide p-toluenesulfonate, and
2-amino-4-fluorobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide methanesulfonate,
a pharmaceutically acceptable salt thereof or a prodrug thereof.

10. The indole compound of 1 above, which is selected from the group consisting of
benzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,
2-aminobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,
2-hydroxybenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,
3-(2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenylcarbamoyloxy)-2,2-dimethylpropionic acid,
benzoic acid 2-(5-chloro-1H-indole-2-carbonyl)-1-methylhydrazide,
benzoic acid 2-(1-acetyl-5-chloro-1H-indole-2-carbonyl)hydrazide,
5-chloro-1H-indole-2-carboxylic acid 2-(imino-phenyl-methyl)hydrazide,
5-aminothiazole-4-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,
benzoic acid 2-(5-fluoro-1H-indole-2-carbonyl)hydrazide,
cyclohexanecarboxylic acid 2-(5-fluoro-1H-indole-2-carbonyl)hydrazide,
thiophene-2-carboxylic acid 2-(5-fluoro-1H-indole-2-carbonyl)hydrazide,
4-nitrobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,
2-methylbenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,
4-methylbenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2-methoxybenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

3-methoxybenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

4-methoxybenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

3-methylbenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2-chlorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

3-chlorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

4-chlorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

4-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)benzoic acid methyl ester,

cyclohexanecarboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2,4-dichlorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2,6-dichlorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2,4-difluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

biphenyl-2-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

3-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

3-trifluoromethylbenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

4-trifluoromethylbenzoic acid 2-(5-chloro-1H-indole-2-

carbonyl)hydrazide,

2-trifluoromethylbenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

benzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide,

benzoic acid 2-(5-chloro-3-methyl-1H-indole-2-carbonyl)hydrazide,

benzoic acid 2-(5,7-dichloro-1H-indole-2-carbonyl)hydrazide,

2-aminobenzoic acid 2-(5-isopropyl-1H-indole-2-carbonyl)hydrazide,

2-amino-4-fluorobenzoic acid 2-(5-isopropyl-1H-indole-2-carbonyl)hydrazide,

2-aminobenzoic acid 2-(5-fluoro-1H-indole-2-carbonyl)hydrazide,

2-aminobenzoic acid 2-(6-chloro-1H-indole-2-carbonyl)hydrazide,

3-amino-4-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)benzoic acid methyl ester,

3-aminoisonicotinic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

isonicotinic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

nicotinic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

pyridine-2-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

3-(dimethylamino)benzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

N-(3-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenyl)acetamide,

N-(2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenyl)acetamide,

4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)-2-methylhydrazide,

2-(2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenoxy)acetic acid methyl ester,

2-(2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenoxy)acetic acid,

2-(dimethylamino)benzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenoxy-N,N-dimethylacetamide,

2-methylaminobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2-amino-4-chlorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2-amino-6-chlorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2-amino-3-chlorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2-amino-5-chlorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

4-cyanobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

4-(1H-tetrazol-5-yl)benzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

3-(1H-tetrazol-5-yl)benzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2-(2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)anilino)acetic acid,

2-aminobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide,

2-amino-4-fluorobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide,

methyl (2-(2-(5-methyl-1H-indole-2-carbonyl)hydrazinocarbonyl)phenyl)carbamate,

2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenyl dimethylcarbamate,

2-aminobenzoic acid 2-(5-ethyl-1H-indole-2-carbonyl)hydrazide,

2-amino-4,5-difluorobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide,

2-(2-hydroxyethoxy)benzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2-(3-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenoxy)acetic acid methyl ester,

2-(3-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenoxy)acetic acid,

2-(3-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenoxy)-N,N-dimethylacetamide,

2-methylthiazole-4-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

4-(2H-[1,2,4]triazol-3-yl)benzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

3-(2H-[1,2,4]triazol-3-yl)benzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1,3-dihydroxy-2-propyl (2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenyl)carbamate,

3-((2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenyl)carbamoyloxy)-2,2-dimethylpropionic acid,

thiophene-2-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

furan-2-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2,6-dichloronicotinic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1H-pyrrole-2-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1H-imidazole-4-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

pyrazine-2-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

thiophene-3-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

furan-3-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

5-chlorothiophene-2-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

3-chlorothiophene-2-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-methyl-1H-pyrrole-2-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

5-methylthiophene-2-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

3-methylthiophene-2-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2,6-difluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2,3-difluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

5-chloro-1H-indole-2-carboxylic acid 2-(naphthalene-1-carbonyl)hydrazide,

3,4,5-trifluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2,3,4,5-tetrafluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2-amino-4-methylbenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2-amino-4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2-amino-5-methylbenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2-amino-6-methylbenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2-amino-3-methylbenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2-amino-4,5-difluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

3-aminothiophene-2-carboxylic acid 2-(5-chloro-1H-indole-2-

carbonyl)hydrazide,

2-aminobenzoic acid 2-(5-bromo-1H-indole-2-carbonyl)hydrazide,

2-amino-4-fluorobenzoic acid 2-(5-bromo-1H-indole-2-carbonyl)hydrazide,

1H-pyrazole-4-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

methyl (2-(2-(5-fluoro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenyl)carbamate,

1-methyl-1H-pyrrole-2-carboxylic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide,

thiophene-3-carboxylic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide,

4H-thieno[3,2-b]pyrrole-5-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

phenyl (2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenyl)carbamate,

benzyl (2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenyl)carbamate,

2-hydroxyethyl (2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenyl)carbamate,

3-hydroxypropyl (2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenyl)carbamate,

2-((2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenyl)carbamoyloxy)acetic acid,

2-((2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenyl)carbamoyloxymethyl)-2-methylmalonic acid,

methyl 2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenylcarbamate,

cyclohexanecarboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)-1-methylhydrazide,

thiophene-2-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)-1-methylhydrazide,

benzoic acid 2-(1H-indole-2-carbonyl)hydrazide,

benzoic acid 2-(5-chloro-1-methyl-1H-indole-2-carbonyl)hydrazide,

benzoic acid 2-(5-methoxy-1H-indole-2-carbonyl)hydrazide,

benzoic acid 2-(5-isopropyl-1H-indole-2-carbonyl)hydrazide,

benzoic acid 2-(5-nitro-1H-indole-2-carbonyl)hydrazide,

benzoic acid 2-(5-benzyloxy-1H-indole-2-carbonyl)hydrazide,

benzoic acid 2-(6-chloro-1H-indole-2-carbonyl)hydrazide,

6H-thieno[2,3-b]pyrrole-5-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

5-chloro-1H-indole-2-carboxylic acid 2-((2-fluorophenyl)-imino-methyl)hydrazide,

5-chloro-1H-indole-2-carboxylic acid 2-((3-fluorophenyl)-imino-methyl)hydrazide,

5-chloro-1H-indole-2-carboxylic acid 2-((4-fluorophenyl)-imino-methyl)hydrazide,

5-chloro-1H-indole-2-carboxylic acid 2-(imino-(p-tolyl)-methyl)hydrazide,

5-chloro-1H-indole-2-carboxylic acid 2-((4-chlorophenyl)-imino-methyl)hydrazide,

5-chloro-1H-indole-2-carboxylic acid 2-((3-chlorophenyl)-imino-methyl)hydrazide,

5-chloro-1H-indole-2-carboxylic acid 2-((3-fluorophenyl)-imino-methyl)hydrazide,

5-chloro-1H-indole-2-carboxylic acid 2-(imino-(o-tolyl)-methyl)hydrazide,

5-chloro-1H-indole-2-carboxylic acid 2-(imino-(m-tolyl)-methyl)hydrazide,

5-chloro-1H-indole-2-carboxylic acid 2-(imino-(thiophen-2-yl)-methyl)hydrazide,

5-chloro-1H-indole-2-carboxylic acid 2-(imino-(pyridin-2-yl)-methyl)hydrazide,

5-chloro-1H-indole-2-carboxylic acid 2-((furan-2-yl)-imino-

methyl)hydrazide,

5-chloro-1H-indole-2-carboxylic acid 2-((2-chloro-6-fluorophenyl)-imino-methyl)hydrazide,

5-chloro-1H-indole-2-carboxylic acid 2-(imino-(2-trifluoromethylphenyl)-methyl)hydrazide,

5-chloro-1H-indole-2-carboxylic acid 2-(imino-(pyrazin-2-yl)-methyl)hydrazide,

3-aminobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

3-methoxybenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

5-amino-2-methylthiazole-4-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2-morpholinoethyl (2-((2-(5-chloro-1H-indole-2-carbonyl)hydrazino)carbonyl)phenyl)carbamate p-toluenesulfonate,

2-amino-4,5-difluorobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide benzenesulfonate,

2-amino-4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide benzenesulfonate,

3-(dimethylamino)benzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide methanesulfonate,

2-amino-4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide hydrochloride,

2-amino-4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide p-toluenesulfonate,

2-amino-4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide p-toluenesulfonate,

2-amino-4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide p-toluenesulfonate,

2-amino-4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide p-toluenesulfonate,

2-aminobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide p-toluenesulfonate,

2-aminobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide benzenesulfonate,

2-amino-4-fluorobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide benzenesulfonate,

3-aminobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide p-toluenesulfonate,

5-chloro-1H-indole-2-carboxylic acid 2-((2-chlorophenyl)-imino-methyl)hydrazide methanesulfonate,

5-chloro-1H-indole-2-carboxylic acid 2-((2-chlorophenyl)-imino-methyl)hydrazide p-toluenesulfonate,

5-chloro-1H-indole-2-carboxylic acid 2-((2-chlorophenyl)-imino-methyl)hydrazide hydrochloride,

5-chloro-1H-indole-2-carboxylic acid 2-(imino-phenyl-methyl)hydrazide methanesulfonate,

5-chloro-1H-indole-2-carboxylic acid 2-((2-chlorophenyl)-imino-methyl)hydrazide butenedioic acid salt,

5-chloro-1H-indole-2-carboxylic acid 2-((2-fluorophenyl)-imino-methyl)hydrazide hydrochloride,

5-chloro-1H-indole-2-carboxylic acid 2-((2-fluorophenyl)-imino-methyl)hydrazide methanesulfonate,

5-chloro-1H-indole-2-carboxylic acid 2-((1-imino-2-phenylethyl)hydrazide methanesulfonate,

5-chloro-1H-indole-2-carboxylic acid 2-((3-fluorophenyl)-imino-methyl)hydrazide hydrochloride,

5-chloro-1H-indole-2-carboxylic acid 2-((3,4-difluorophenyl)-imino-methyl)hydrazide methanesulfonate,

5-chloro-1H-indole-2-carboxylic acid 2-(imino-(2-methoxyphenyl)-methyl)hydrazide methanesulfonate,

5-chloro-1H-indole-2-carboxylic acid 2-((2,6-difluorophenyl)-imino-methyl)hydrazide methanesulfonate,

5-chloro-1H-indole-2-carboxylic acid 2-((2,4-difluorophenyl)-imino-methyl)hydrazide methanesulfonate,

5-chloro-1H-indole-2-carboxylic acid 2-((1,2-dimethyl-1H-

pyrrol-5-yl)-imino-methyl)hydrazide methanesulfonate,
2-aminobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide p-toluenesulfonate,
2-aminobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide benzenesulfonate,
2-amino-4-fluorobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide benzenesulfonate,
2-(dimethylamino)benzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide p-toluenesulfonate,
2-amino-4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide methanesulfonate,
2-aminobenzoic acid 2-(5-bromo-1H-indole-2-carbonyl)hydrazide methanesulfonate,
2-amino-4-fluorobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide p-toluenesulfonate, and
2-amino-4-fluorobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide methanesulfonate
a pharmaceutically acceptable salt thereof or a prodrug thereof.

11. The indole compound of 1 above, which is selected from the group consisting of
2-morpholinoethyl (2-((2-(5-chloro-1H-indole-2-carbonyl)hydrazino)carbonyl)phenyl)carbamate p-toluenesulfonate,
2-amino-4,5-difluorobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide benzenesulfonate,
2-amino-4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide benzenesulfonate,
3-(dimethylamino)benzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide methanesulfonate,
2-amino-4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide hydrochloride,
2-amino-4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-

carbonyl)hydrazide p-toluenesulfonate,

2-amino-4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide p-toluenesulfonate,

2-amino-4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide p-toluenesulfonate,

2-amino-4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide p-toluenesulfonate,

2-aminobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide p-toluenesulfonate,

2-aminobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide benzenesulfonate,

2-amino-4-fluorobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide benzenesulfonate,

3-aminobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide p-toluenesulfonate,

5-chloro-1H-indole-2-carboxylic acid 2-((2-chlorophenyl)-imino-methyl)hydrazide methanesulfonate,

5-chloro-1H-indole-2-carboxylic acid 2-((2-chlorophenyl)-imino-methyl)hydrazide p-toluenesulfonate,

5-chloro-1H-indole-2-carboxylic acid 2-((2-chlorophenyl)-imino-methyl)hydrazide hydrochloride,

5-chloro-1H-indole-2-carboxylic acid 2-(imino-phenyl-methyl)hydrazide methanesulfonate,

5-chloro-1H-indole-2-carboxylic acid 2-((2-chlorophenyl)-imino-methyl)hydrazide butenedioic acid salt ,

5-chloro-1H-indole-2-carboxylic acid 2-((2-fluorophenyl)-imino-methyl)hydrazide hydrochloride,

5-chloro-1H-indole-2-carboxylic acid 2-((2-fluorophenyl)-imino-methyl)hydrazide methanesulfonate,

5-chloro-1H-indole-2-carboxylic acid 2-((1-imino-2-phenylethyl)hydrazide methanesulfonate,

5-chloro-1H-indole-2-carboxylic acid 2-((3-fluorophenyl)-imino-methyl)hydrazide hydrochloride,

5-chloro-1H-indole-2-carboxylic acid 2-((3,4-difluorophenyl)-imino-methyl)hydrazide methanesulfonate,

5-chloro-1H-indole-2-carboxylic acid 2-(imino-(2-methoxyphenyl)-methyl)hydrazide methanesulfonate,

5-chloro-1H-indole-2-carboxylic acid 2-((2,6-difluorophenyl)-imino-methyl)hydrazide methanesulfonate,

5-chloro-1H-indole-2-carboxylic acid 2-((2,4-difluorophenyl)-imino-methyl)hydrazide methanesulfonate,

5-chloro-1H-indole-2-carboxylic acid 2-((1,2-dimethyl-1H-pyrrol-5-yl)-imino-methyl)hydrazide methanesulfonate,

2-aminobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide p-toluenesulfonate,

2-aminobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide benzenesulfonate,

2-amino-4-fluorobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide benzenesulfonate,

2-(dimethylamino)benzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide p-toluenesulfonate,

2-amino-4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide methanesulfonate,

2-aminobenzoic acid 2-(5-bromo-1H-indole-2-carbonyl)hydrazide methanesulfonate,

2-amino-4-fluorobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide p-toluenesulfonate, and

2-amino-4-fluorobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide methanesulfonate

a pharmaceutically acceptable salt thereof or a prodrug thereof.

12. A pharmaceutical composition comprising an indole compound of any of the above-mentioned 1 to 11, a pharmaceutically acceptable salt thereof or a prodrug thereof, and a pharmaceutically acceptable carrier.

13. An HLGPa inhibitor comprising an indole compound of any of

the above-mentioned 1 to 11, a pharmaceutically acceptable salt thereof or a prodrug thereof, and a pharmaceutically acceptable carrier.

14. A therapeutic agents for diabetes, which comprises an indole compound of any of the above-mentioned 1 to 11, a pharmaceutically acceptable salt thereof or a prodrug thereof, and a pharmaceutically acceptable carrier.

15. The pharmaceutical composition of the above-mentioned 14, which is used together with a therapeutic agent for hyperlipidemia.

16. The pharmaceutical composition of the above-mentioned 15, wherein the therapeutic agent for hyperlipidemia is a statin pharmaceutical agent.

17. The pharmaceutical composition of the above-mentioned 16, wherein the statin pharmaceutical agent is lovastatin, simvastatin, pravastatin, fluvastatin, atorvastatin or cerivastatin.

18. A pharmaceutical composition for the treatment or prophylaxis of diabetes, which comprises a therapeutic agent for diabetes selected from the group consisting of insulin preparations, sulfonylurea agents, insulin secretagogues, sulfonamides, biguanides, α-glucosidase inhibitors and insulin sensitizers, and an HLGPa inhibitor in combination.

19. The pharmaceutical composition of claim 18, wherein the therapeutic agent for diabetes is selected from the group consisting of insulin, glibenclamide, torbutamide, glyclopyramide, acetohexamide, glimepiride, tolazamide, gliclazide, nateglinide, glybuzole, metformin hydrochloride, buformin hydrochloride, voglibose, acarbose and pioglitazone hydrochloride.

20. The therapeutic agent for diabetes of the above-mentioned 18 or 19, wherein the HLGPa inhibitor is an indole compound of any of the above-mentioned 1 to 11, a pharmaceutically

acceptable salt thereof or a prodrug thereof.

21. A method for treating or preventing diabetes, which comprises administering an indole compound of any of the above-mentioned 1 to 11, a pharmaceutically acceptable salt thereof or a prodrug thereof.

22. The method of the above-mentioned 21, which comprises using a therapeutic agent for hyperlipidemia in combination.

23. The method of the above-mentioned 22, wherein the therapeutic agent for hyperlipidemia is a statin pharmaceutical agent.

24. The method of the above-mentioned 23, wherein the statin pharmaceutical agent is lovastatin, simvastatin, pravastatin, fluvastatin, atorvastatin or cerivastatin.

25. A method for treating or preventing diabetes, which comprises administering a pharmaceutical composition for the treatment or prophylaxis of diabetes comprising a therapeutic agent for diabetes selected from the group consisting of insulin preparations, sulfonylurea agents, insulin secretagogues, sulfonamides, biguanides, α-glucosidase inhibitors and insulin sensitizers, and an HLGPa inhibitor in combination.

26. The method of the above-mentioned 25, wherein the therapeutic agent for diabetes is selected from the group consisting of insulin, glibenclamide, torbutamide, glyclopyramide, acetohexamide, glimepiride, tolazamide, gliclazide, nateglinide, glybuzole, metformin hydrochloride, buformin hydrochloride, voglibose, acarbose and pioglitazone hydrochloride.

27. The method of the above-mentioned 25 or 26, wherein the HLGPa inhibitor is an indole compound of any of the above-mentioned 1 to 11, a pharmaceutically acceptable salt thereof or a prodrug thereof.

28. Use of an indole compound of any of the above-mentioned 1

to 11, a pharmaceutically acceptable salt thereof or a prodrug thereof for the production of a therapeutic agent for diabetes.

29. The use of the above-mentioned 28, which comprises use of a therapeutic agent for hyperlipidemia in combination.

30. The use of the above-mentioned 29, wherein the therapeutic agent for hyperlipidemia is a statin pharmaceutical agent.

31. The use of the above-mentioned 30, wherein the statin pharmaceutical agent is lovastatin, simvastatin, pravastatin, fluvastatin, atorvastatin or cerivastatin.

32. Use of a therapeutic agent for diabetes selected from the group consisting of selected from the group consisting of insulin preparations, sulfonylurea agents, insulin secretagogues, sulfonamides, biguanides, α-glucosidase inhibitors and insulin sensitizers and an HLGPa inhibitor for the production of a pharmaceutical composition for the treatment or prophylaxis of diabetes.

33. The use of the above-mentioned 32, wherein the therapeutic agent for diabetes is selected from the group consisting of insulin, glibenclamide, torbutamide, glyclopyramide, acetohexamide, glimepiride, tolazamide, gliclazide, nateglinide, glybuzole, metformin hydrochloride, buformin hydrochloride, voglibose, acarbose and pioglitazone hydrochloride.

34. The use of the above-mentioned 32 or 33, wherein the HLGPa inhibitor is an indole compound of any of the above-mentioned 1 to 11, a pharmaceutically acceptable salt thereof or a prodrug thereof.

Embodiment of the Invention

The definition of each substituent used in the present specification is as follows.

The "halogen atom" is a chlorine atom, a bromine atom, a fluorine atom and the like. For R^2, it is preferably a chlorine atom, for R^3, it is preferably a chlorine atom, a

bromine atom or a fluorine atom, for R^{11}, R^{12}, R^{13}, R^{14} or R^{15}, it is preferably a chlorine atom or a fluorine atom, for R^{16b}-R^{16n} or R^{17b}-R^{17n}, it is preferably a chlorine atom, and for R^{36} or R^{37}, it is preferably a chlorine atom or a fluorine atom.

The "C_{1-6} alkyl group" is a straight chain or branched chain alkyl group having 1 to 6 carbon atoms, such as methyl group, ethyl group, propyl group, isopropyl group, butyl group, isobutyl group, sec-butyl group, tert-butyl group, pentyl group, isopentyl group, neopentyl group, tert-pentyl group, hexyl group and the like. Preferred is a straight chain or branched chain alkyl group having 1 to 4 carbon atoms, and particularly preferred are methyl group, ethyl group and isopropyl group. For R^1, it is preferably a methyl group, for R^3, it is preferably a methyl group, an ethyl group or an isopropyl group, for R^4, it is preferably a methyl group, for R^5, it is preferably a methyl group, for R^6, it is preferably a methyl group, for R^8, it is preferably a methyl group, for R^9 or R^{10}, it is preferably a methyl group, for R^{11}, R^{12}, R^{13}, R^{14} or R^{15}, it is preferably a methyl group, for R^{16b}-R^{16n} or R^{17b}-R^{17n}, it is preferably a methyl group, for R^{20} or R^{21}, it is preferably a methyl group or an ethyl group, for R^{25} or R^{26}, it is preferably a methyl group or an ethyl group, for R^{28} or R^{29}, it is preferably a methyl group or an ethyl group, for R^{30}, it is preferably a methyl group, an ethyl group, a propyl group, an isopropyl group, a butyl group, an isobutyl group, a sec-butyl group, a tert-butyl group, a pentyl group, an isopentyl group, a neopentyl group or a tert-pentyl group, for R^{31}, $R^{31'}$, R^{32} or $R^{32'}$, it is preferably a methyl group or an ethyl group, for R^{33}, it is preferably a methyl group, for R^{35}, it is preferably a methyl group, for R^{36} or R^{37}, it is preferably a methyl group, for R^{39} or R^{40}, it is preferably a methyl group, for R^{41}, it is preferably a methyl group, for R^{42}, $R^{42'}$, $R^{42''}$ or R^{43}, it is preferably a methyl group, for R^{44} or $R^{44'}$, it is

preferably a methyl group, an ethyl group, a propyl group or an isopropyl group, and for R^{45}, it is preferably a methyl group.

The "C_{1-6} alkyl group" for R^{30} may be substituted by a hydroxyl group, a trifluoromethyl group, an aryl group optionally having substituents (hereinafter as defined for "aryl group", preferably phenyl group), morpholino group or carboxyl group, wherein the position of substitution is not particularly limited as long as substitution is possible. As the C_{1-6} alkyl group substituted by hydroxyl group, trifluoromethyl group, aryl group optionally having substituents, morpholino group or carboxyl group, for example, 2-hydroxyethyl group, 3-hydroxypropyl group, 4-hydroxybutyl group, 2,3-dihydroxylpropyl group; 2-carboxypropyl group, 2,2-dicarboxypropyl group; 2,2,2-trifluoroethyl group; benzyl group; morpholinomethyl group and the like can be mentioned, with preference given to 2,3-dihydroxypropyl group and 2,2-dicarboxypropyl group.

The "C_{1-6} alkyl group" for R^{44} and $R^{44'}$ may be substituted by a carboxyl group or a C_{2-7} alkoxycarbonyl group (as defined below), wherein the position of substitution is not particularly limited as long as substitution is possible. The C_{1-6} alkyl group substituted by a carboxyl group or a C_{2-7} alkoxycarbonyl group is preferably a carboxymethyl group or a methoxycarbonylmethyl group.

The "C_{1-6} alkoxy group" is a straight chain or branched chain alkoxy group having 1 to 6 carbon atoms, such as methoxy group, ethoxy group, propoxy group, isopropoxy group, butoxy group, tert-butoxy group, pentyloxy group, tert-pentyloxy group and hexyloxy group. Preferred is a straight chain or branched chain alkoxy group having 1 to 4 carbon atoms, such as methoxy group, ethoxy group, isopropoxy group, butoxy group, tert-butoxy group, and particularly preferred are methoxy

group and ethoxy group. For R^3, it is preferably a methoxy group, for R^{11}, R^{12}, R^{13}, R^{14} or R^{15}, it is preferably a methoxy group or an ethoxy group, for R^{16b}-R^{16n} or R^{17b}-R^{17n}, it is preferably a methoxy group, for R^{19}, it is preferably a methoxy group, for R^{22} or $R^{22'}$, it is preferably a methoxy group, for R^{24}, it is preferably a methoxy group, an ethoxy group, a propoxy group or an isopropoxy group, for R^{34}, it is preferably a methoxy group, for R^{36} or R^{37}, it is preferably a methoxy group, and for R^{39} or R^{40}, it is preferably a methoxy group.

The "C_{2-7} alkoxycarbonyl group" is a linear or branched chain alkoxycarbonyl group wherein the alkyl moiety has 1 to 6 (preferably 1 to 4) carbon atoms. Examples thereof include methoxycarbonyl group, ethoxycarbonyl group, propoxycarbonyl group, isopropoxycarbonyl group, butoxycarbonyl group, isobutoxycarbonyl group, tert-butoxycarbonyl group, pentyloxycarbonyl group, hexyloxycarbonyl group and the like. Preferred are methoxycarbonyl group, ethoxycarbonyl group and tert-butoxycarbonyl group. For R^5, it is preferably a methoxycarbonyl group, for R^{18}, it is preferably a methoxycarbonyl group or a tert-butoxycarbonyl group, for R^{36} or R^{37}, it is preferably a methoxycarbonyl group, for R^{39} or R^{40}, it is preferably a methoxycarbonyl group, and for R^{44} or $R^{44'}$, it is preferably a methoxycarbonyl group.

The "C_{2-7} alkoxycarbonylamino group" is a linear or branched chain alkoxycarbonylamino group wherein the alkyl moiety has 1 to 6 (preferably 1 to 4) carbon atoms. Examples thereof include methoxycarbonylamino group, ethoxycarbonylamino group, propoxycarbonylamino group, isopropoxycarbonylamino group, butoxycarbonylamino group, isobutoxycarbonylamino group, tert-butoxycarbonylamino group, pentyloxycarbonylamino group, hexyloxycarbonylamino and the like. Preferred are methoxycarbonylamino group, ethoxycarbonylamino group and tert-butoxycarbonylamino group.

For R^9 or R^{10}, it is preferably a methoxycarbonyl group or a tert-butoxycarbonylamino group, and for R^{22} or $R^{22'}$, it is preferably a tert-butoxycarbonylamino group.

The "C_{3-13} alkoxycarbonylalkyl group" is a linear or branched chain alkoxycarbonylalkyl group wherein the both alkyl moieties (alkoxy moiety and alkyl moiety) have 1 to 6 (preferably 1 to 4) carbon atoms. Examples thereof include methoxycarbonylmethyl group, methoxycarbonylethyl group, ethoxycarbonylmethyl group, ethoxycarbonylethyl group, propoxycarbonylmethyl group, isopropoxycarbonylmethyl group, butoxycarbonylmethyl group, isobutoxycarbonylmethyl group, tert-butoxycarbonylmethyl group, pentyloxycarbonylmethyl group, hexyloxycarbonylmethyl and the like. Preferred are methoxycarbonylmethyl group, ethoxycarbonylmethyl group and tert-butoxycarbonylmethyl group. For R^{20} and R^{21}, it is preferably a methoxycarbonylmethyl group.

The "C_{2-7} alkylcarbonyloxy group" is a linear or branched chain alkylcarbonyloxy group wherein the alkyl moiety has 1 to 6 (preferably 1 to 4) carbon atoms. Examples thereof include methylcarbonyloxy group, ethylcarbonyloxy group, propylcarbonyloxy group, isopropylcarbonyloxy group, butylcarbonyloxy group, isobutylcarbonyloxy group, tert-butylcarbonyloxy group, pentylcarbonyloxy group, hexylcarbonyloxy and the like. Preferred are methylcarbonyloxy group, ethylcarbonyloxy group and tert-butylcarbonyloxy group. For R^{23}, it is preferably a methylcarbonyloxy group, and for R^{34}, it is preferably a methylcarbonyloxy group.

The "C_{1-6} hydroxyalkyl group" is a straight chain or branched chain alkyl group having 1 to 6 (preferably 1 to 4) carbon atoms, which is substituted by one or more hydroxyl groups, wherein the position of substitution of the hydroxyl group is not particularly limited. For example, hydroxymethyl group; 1- or 2-hydroxyethyl group; 1-, 2- or 3-hydroxypropyl

group; 1-, 2-, 3- or 4-hydroxybutyl group; 1-, 2-, 3-, 4- or 5-hydroxypentyl group; 1-, 2-, 3-, 4-, 5- or 6-hydroxyhexyl group; 2-hydroxy-2-methylethyl group; 1,2-dihydroxyethyl group and the like can be mentioned, with preference given to 2-hydroxyethyl group and 1,2-dihydroxyethyl group. For R^9 or R^{10}, it is preferably a hydroxymethyl group.

The "C_{1-6} haloalkyl group" is a straight chain or branched chain alkyl group having 1 to 6 (preferably 1 to 4) carbon atoms, which is substituted by one or more halogen atoms (as defined above), wherein the position of substitution of the hydroxyl group is not particularly limited. For example, trifluoromethyl group, 1- or 2-chloroethyl group, 1- or 2-bromomethyl group, 1- or 2-fluoroethyl group, 1-, 2- or 3-chloropropyl group, 1-, 2- or 3-bromopropyl group, 1-, 2- or 3-fluoropropyl group, 1-, 2-, 3- or 4-chlorobutyl group, 1-, 2-, 3- or 4-bromobutyl group, 1-, 2-, 3- or 4-fluorobutyl group and the like can be mentioned, with preference given to trifluoromethyl group. For R^{11}, R^{12}, R^{13}, R^{14} or R^{15}, it is preferably a trifluoromethyl group.

The "C_{1-6} alkylamino group" is an amino group monosubstituted by a straight chain or branched chain alkyl group having 1 to 6 (preferably 1 to 4) carbon atoms, such as methylamino group, ethylamino group, propylamino group, butylamino group, pentylamino group, hexylamino group and the like. Preferred are methylamino group and ethylamino group. For R^{27}, it is preferably a methylamino group or an ethylamino group, for R^{34}, it is preferably a methylamino group, and for R^{41}, it is preferably a methylamino group or an ethylamino group.

The "C_{2-12} dialkylamino group" is an amino group disubstituted by straight chain or branched chain alkyl groups having 1 to 6 (preferably 1 to 4) carbon atoms, wherein the alkyl moiety may be the same or different. For example,

dimethylamino group, diethylamino group, dipropylamino group, dibutylamino group, dipentylamino group, dihexylamino group and the like can be mentioned, with preference given to dimethylamino group and diethylamino group. For R^{22} or $R^{22'}$, it is preferably a dimethylamino group, for R^{27}, it is preferably a dimethylamino group, for R^{34}, it is preferably a dimethylamino group, and for R^{41}, it is preferably a dimethylamino group.

The "C_{3-7} cycloalkyl group" is a cycloalkyl group having 3 to 7 (preferably 3 to 6) carbon atoms. Specific examples include cyclopropyl group, cyclobutyl group, cyclopentyl group, cyclohexyl group, cycloheptyl group and the like. Preferred are cycloalkyl group having 3 to 6 carbon atoms. Specific examples include cyclopropyl group, cyclobutyl group, cyclopentyl group and cyclohexyl group. Particularly preferred are cyclopropyl group and cyclohexyl group. For R^{9} or R^{10}, it is preferably a cyclopropyl group, a cyclopentyl group or a cyclohexyl group.

The "acyl group" is an alkylcarbonyl group such as acetyl group, propionyl group, butyryl group, pivaloyl group and the like wherein the alkyl moiety preferably has 1 to 6, more preferably 1 to 4 carbon atoms and is a linear or branched chain; an arylcarbonyl group such as benzoyl group, naphthoyl and the like wherein the aryl moiety preferably has 6 to 12, more preferably 6 to 10 carbon atoms; and the like, with preference given to acetyl group. For R^{1}, it is preferably an acetyl group, for R^{3}, it is preferably an acetyl group, and for R^{28} or R^{29}, it is preferably an acetyl group.

The "aryl group" preferably has 6 to 12, more preferably 6 to 10 carbon atoms, such as phenyl group, naphthyl group and the like, with preference given to phenyl group. The aryl group may be substituted by 1 to 6 the same or different substituents selected from phenyl group, haloalkyl group

(those similar to the above-mentioned "C_{1-6} haloalkyl group" can be mentioned), halogen atom (as defined above), C_{1-6} alkyl group (as defined above), C_{1-6} alkoxy group (as defined above), C_{2-7} alkoxycarbonyl group (as defined above), nitro group, cyano group, carboxyl group, hydroxyl group, amino group, C_{1-6} alkylamino group (as defined above) and diC_{1-6} alkylamino group (as defined for the above-mentioned "C_{2-12} dialkylamino group"), wherein the position of substituent may be any and is not particularly limited. The phenyl group in the above-mentioned substituents may be further substituted by 1 to 6 the same or different substituents selected from the above-mentioned substituent group except phenyl group. To be concrete, phenyl group substituted by the following same or different 1 to 3 substituents is preferable. Examples of the substituents: haloalkyl groups such as trifluoromethyl group etc.; halogen atoms such as chlorine atom, bromine atom, fluorine atom etc.; C_{1-6} alkyl groups such as methyl group, ethyl group, propyl group, isopropyl group, butyl group, tert-butyl group etc.; C_{1-6} alkoxy groups such as methoxy group, ethoxy group, propoxy group, isopropoxy group, butoxy group, isobutoxy group, sec-butoxy group, tert-butoxy group etc.; C_{2-7} alkoxycarbonyl groups such as methoxycarbonyl group, ethoxycarbonyl group, propoxycarbonyl group etc.; nitro group; cyano group; carboxyl group; hydroxyl group; amino group; C_{1-6} alkylamino groups such as methylamino group, ethylamino group, propylamino group, butylamino group etc.; di-C_{1-6} alkylamino groups such as dimethylamino group, diethylamino group, dipropylamino group etc.; and the like. For R^8, it is preferably a phenyl group, for R^{11}, R^{12}, R^{13}, R^{14} or R^{15}, it is preferably a phenyl group, for R^{19}, it is preferably a phenyl group, for R^{28} or R^{29}, it is preferably a phenyl group, for R^{31}, R^{30}, $R^{31'}$, R^{32} or $R^{32'}$, it is preferably a phenyl group, for R^{33}, it is preferably a phenyl group, for R^{38}, it is preferably phenyl group optionally

substituted by a halogen atom or C_{1-6} alkyl group (particularly, phenyl group, chlorophenyl group, fluorophenyl group, tolyl group), for R^{42}, $R^{42'}$, $R^{42''}$ or R^{43}, it is preferably a phenyl group, for R^{45}, it is preferably phenyl group optionally substituted by a halogen atom (particularly, phenyl group, fluorophenyl group), and for R^{46} or $R^{46'}$, it is preferably phenyl group optionally substituted by a halogen atom, a hydroxy group or C_{1-6} alkoxy group (particularly, phenyl group, fluorophenyl group, chlorophenyl group, hydroxyphenyl group, methoxyphenyl group).

The "aryloxy group" preferably has 6 to 12, more preferably 6 to 10, carbon atoms, such as phenoxy group, naphthyloxy group and the like. Preferred is phenoxy group. The aryl group of the aryloxy group may be substituted by 1 to 6 the same or different substituents selected from phenyl group, haloalkyl group (those similar to the above-mentioned "C_{1-6} haloalkyl group" can be mentioned), halogen atom (as defined above), C_{1-6} alkyl group (as defined above), C_{1-6} alkoxy group (as defined above), C_{2-7} alkoxycarbonyl group (as defined above), nitro group, cyano group, carboxyl group, hydroxyl group, amino group, C_{1-6} alkylamino group (as defined above) and diC_{1-6} alkylamino group (as defined for the above-mentioned "C_{2-12} dialkylamino group"). The phenyl group in the above-mentioned substituents may be further substituted by 1 to 6 the same or different substituents selected from the above-mentioned substituent group except phenyl group. For R^{11}, R^{12}, R^{13}, R^{14} or R^{15}, it is preferably a phenoxy group.

The "aralkyl group" is an arylalkyl group wherein the aryl moiety is phenyl group and the alkyl moiety is a straight chain or branched chain alkyl group having 1 to 6 (preferably 1 to 4) carbon atoms, for example, benzyl group, phenylpropyl group, phenylbutyl group, phenylhexyl group and the like. The phenyl group may be further substituted by 1 to 6 the same or

different substituents selected from haloalkyl group (those similar to the above-mentioned "C_{1-6} haloalkyl group" can be mentioned), halogen atom (as defined above), C_{1-6} alkyl group (as defined above), C_{1-6} alkoxy group (as defined above), C_{2-7} alkoxycarbonyl group (as defined above), nitro group, cyano group, carboxyl group, hydroxyl group, amino group, C_{1-6} alkylamino group (as defined above) and di-C_{1-6} alkylamino group (as defined for the above-mentioned "C_{2-12} dialkylamino group"). For R^6, it is preferably a benzyl group or a 4-fluorobenzyl group, for R^{11}, R^{12}, R^{13}, R^{14} or R^{15}, it is preferably a benzyl group or a phenylpropyl group, for R^{20} or R^{21}, it is preferably a benzyl group, for R^{25} or R^{26}, it is preferably a benzyl group, and for R^{46} or $R^{46'}$, it is preferably a benzyl group.

The "aralkyloxy group" is an arylalkoxy group wherein the aryl moiety is phenyl group and alkoxy moiety is a linear or branched chain alkoxy group having 1 to 6 (preferably 1 to 4) carbon atoms, such as benzyloxy group, phenylpropoxy group, phenylbutoxy group, phenylhexyloxy group and the like. The phenyl group may be further substituted by 1 to 6 the same or different substituents selected from haloalkyl group (those similar to the above-mentioned "C_{1-6} haloalkyl group" can be mentioned), halogen atom (as defined above), C_{1-6} alkyl group (as defined above), C_{1-6} alkoxy group (as defined above), C_{2-7} alkoxycarbonyl group (as defined above), nitro group, cyano group, carboxyl group, hydroxyl group, amino group, C_{1-6} alkylamino group (as defined above) and diC_{1-6} alkylamino group (as defined for the above-mentioned "C_{2-12} dialkylamino group"). For R^3, it is preferably a benzyloxy group.

The "acylamino group" has 2 to 13, preferably 2 to 11, carbon atoms, and is exemplified by alkylcarbonylamino having 2 to 7 carbon atoms (e.g., acetylamino, propionylamino, butyrylamino, pivaloylamino and the like) and the like, with preference given to acetylamino.

The "C_{2-7} haloalkylcarbonylamino group" is a haloalkylcarbonylamino group having preferably 2 to 5 carbon atoms, wherein the haloalkyl moiety is as defined for the above-mentioned "C_{1-6} haloalkyl group", with preference given to trifluoromethylcarbonylamino.

The "heteroaryl group" is a heteroaryl group having, besides carbon atom, one or more, preferably 1 to 3, heteroatoms such as nitrogen atom, sulfur atom, oxygen atom and the like, which is preferably a 4- to 7-membered ring, more preferably a 5- or 6-membered ring. Specific examples include thienyl, furyl, imidazolyl, pyrrolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyrazolyl, thioxazolyl, diazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, pyrrolinyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, azepinyloxepinyl and the like. R^{38} is preferably pyridyl, and R^{46} and $R^{46'}$ are preferably thienyl.

The thiazolyl group for R^3 is optionally substituted by a C_{1-6} alkyl group (as defined above) or amino group.

The aralkyl group for R^6 is optionally substituted by a halogen atom (as defined above).

The triazolyl group encompasses both a 1,2,3-form and a 1,2,4-form.

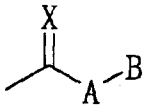
The position of bonding of tetrazolyl group and triazolyl group is not particularly limited as long as the bonding is possible.

The "pharmaceutically acceptable salt" includes, for example, various inorganic acid addition salts such as hydrochloride, hydrobromide, sulfonate, phosphate, nitrate and the like; various organic acid addition salts such as acetate, propionate, succinate, glycolate, lactate, malate, oxalate, tartrate, citrate, maleate, fumarate, methanesulfonate, benzenesulfonate, p-toluenesulfonate, ascorbate and the like; salts with various amino acids such as aspartate, glutamate

and the like. Preferred are hydrochloride, methanesulfonate, benzenesulfonate and p-toluenesulfonate, and particularly preferred is p-toluenesulfonate. In some cases, it may be a water-containing salt, a hydrate or a solvate.

A preferable embodiment of the compound (1) of the present invention is, for example, an embodiment wherein R^6 is a hydrogen atom, a C_{1-6} alkyl group or an aralkyl group wherein the aralkyl group is optionally substituted by a halogen atom;

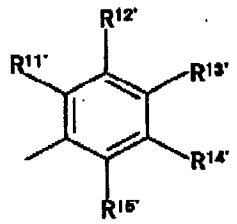
R^7 is



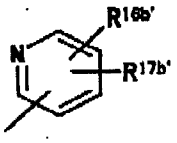
wherein X is =O, =S or =NH;

A is $-N(R^{8'})-$ wherein $R^{8'}$ is a hydrogen atom, a C_{1-6} alkyl group or a phenyl group optionally having substituents, $-C(R^{9'})(R^{10'})-$ wherein $R^{9'}$ and $R^{10'}$ are the same or different and each is a hydrogen atom, a hydroxyl group, an amino group, a C_{1-6} alkyl group, a C_{1-6} hydroxyalkyl group, a C_{2-7} alkoxycarbonylamino group or an acylamino group, or $R^{9'}$ and $R^{10'}$ may form, together with the adjacent carbon atom, a C_{3-7} cycloalkyl group, $-(CH_2)_m-NH-$ wherein m is an integer of 1 to 4), -CO-, -S- or a single bond; and

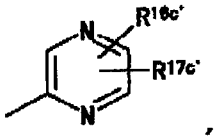
B is



(a')

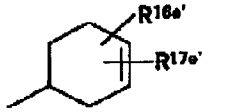


(b')

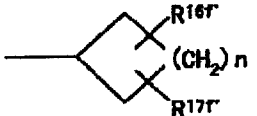


(c')

(d')



(e')



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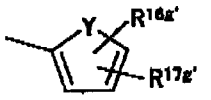

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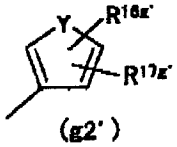
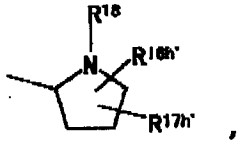


(g2')



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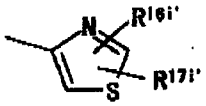
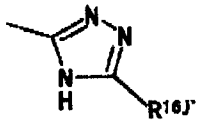


(i')



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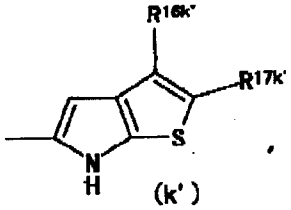
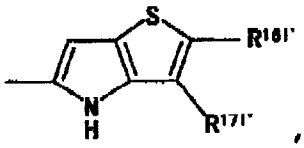
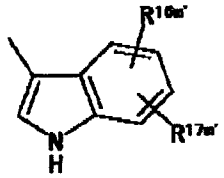


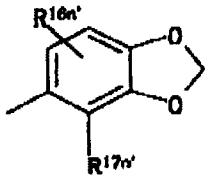
(k')



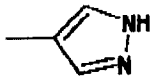
(l')



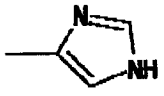
(m')



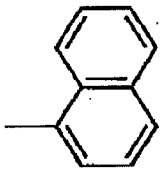
(n')



(o')

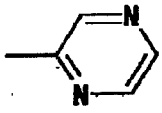


(p')



(q')

or



(r')

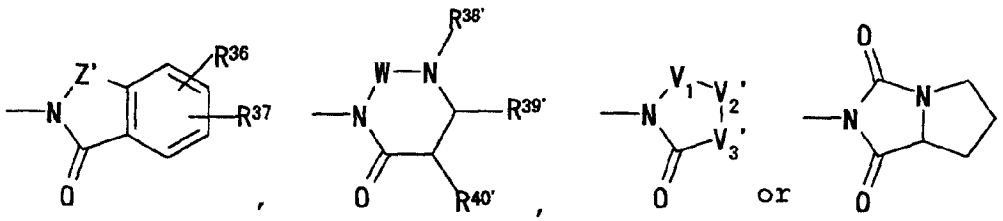
wherein $R^{11'}$, $R^{12'}$, $R^{13'}$, $R^{14'}$ and $R^{15'}$ are the same or different and each is a hydrogen atom, a halogen atom, a C_{1-6} alkyl group, a C_{1-6} alkoxy group, a nitro group, a hydroxyl group, a cyano group, a haloalkyl group, an aralkyl group, a phenyl group optionally having substituents, an aryloxy group, a tetrazolyl group, a triazolyl group, $-(CH_2)_p-CO-R^{19'}$ wherein p is 0 or an

integer of 1 to 4 and $R^{19'}$ is a phenyl group optionally having substituents, a hydroxyl group, a C_{1-6} alkoxy group or -$N(R^{20})(R^{21})$- wherein R^{20} and R^{21} are as defined in the compound (1) of the present invention, $-O-(CH_2)_r-R^{23}$ wherein r and R^{23} are as defined in the compound (1) of the present invention, $-O-CO-R^{27}$ wherein R^{27} is as defined in the compound (1) of the present invention, or $-N(R^{28'})(R^{29'})$ wherein $R^{28'}$ and $R^{29'}$ are the same or different and each is a hydrogen atom, a C_{1-6} alkyl group, a phenyl group optionally having substituents, an acyl group, $-(CH_2)_{p'}-COO-R^{30'}$ wherein p' is as defined in the compound (1) of the present invention and $R^{30'}$ is a hydrogen atom, a phenyl group optionally having substituents or a C_{1-6} alkyl group wherein the C_{1-6} alkyl group is optionally substituted by a hydroxyl group, a trifluoromethyl group, a phenyl group optionally having substituents, a morpholino group or a carboxyl group, $-CON(R^{31''})(R^{32''})$ wherein $R^{31''}$ and $R^{32''}$ are the same or different and each is a hydrogen atom, a C_{1-6} alkyl group or a phenyl group optionally having substituents, $-CO-R^{33'}$ wherein $R^{33'}$ is a C_{1-6} alkyl group or a phenyl group optionally having substituents or $-CO-(CH_2)_{r'}-R^{34}$ wherein r' and R^{34} are as defined in the compound (1) of the present invention,

$R^{16b'}$-$R^{16n'}$ and $R^{17b'}$-$R^{17n'}$ are the same or different and each is a hydrogen atom, a halogen atom, a C_{1-6} alkyl group, an amino group, a hydroxyl group, a C_{1-6} alkoxy group or -$CON(R^{31'''})(R^{32'''})$ wherein $R^{31'''}$ and $R^{32'''}$ are as defined for $R^{31''}$ and $R^{32''}$, and

R^{18}, Y and n are as defined in the compound (1) of the present invention, or

R^6 and R^7 may form, together with the adjacent nitrogen atom,



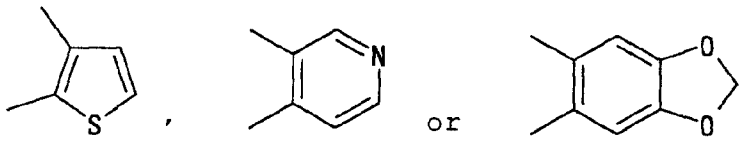
(i') (ii') (iii') (iv)

wherein R^{36} and R^{37} are as defined in the compound (1) of the present invention;

Z' is $-CH_2-CH_2-$, $-C(R^{42})=CH-$, $-C(R^{42'})=N-$, $-N=N-$, $-CO-$, $-CO-O-$, $-CO-CH_2-O-$, $-CH_2-CO-NH-$, $-C(R^{42''})(R^{43})-N(R^{44})-$ wherein R^{42}, $R^{42'}$, $R^{42''}$ and R^{43} are the same or different and each is a hydrogen atom, a C_{1-6} alkyl group or a phenyl group optionally having substituents and R^{44} is as defined in the compound (1) of the present invention or $-C(U)-N(R^{44'})-$ wherein U and $R^{44'}$ are as defined in the compound (1) of the present invention;

$R^{38'}$ is a hydrogen atom, a phenyl group optionally substituted by a halogen atom or a C_{1-6} alkyl group, or a pyridyl group;

$R^{39'}$ and $R^{40'}$ are both hydrogen atoms, or $R^{39'}$ and $R^{40'}$ may form, together with the adjacent carbon atom,



W and V_1 are as defined in the compound (1) of the present invention;

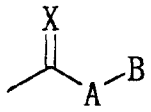
V_2' is $-O-$, $-CH_2-$ or $-N(R^{45})-$ wherein R^{45} is a hydrogen atom, a C_{1-6} alkyl group or a phenyl group optionally substituted by a halogen atom; and

V_3' is $-CH(R^{46})-$ or $-N(R^{46'})-$ wherein R^{46} and $R^{46'}$ are each a hydrogen atom, a benzyl group, a thienyl group, or a phenyl group optionally substituted by a halogen atom, a hydroxy group or a C_{1-6} alkoxy group; and

an embodiment wherein

R^6 is a hydrogen atom, a C_{1-6} alkyl group or an aralkyl group wherein the aralkyl group is optionally substituted by a halogen atom;

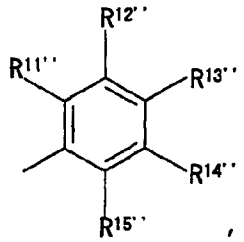
R^7 is

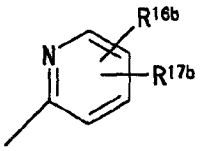


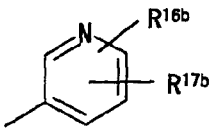
wherein X is as defined in the compound (1) of the present invention;

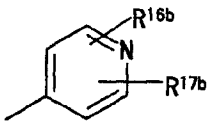
A is $-N(R^{8''})-$ wherein $R^{8''}$ is a hydrogen atom, a C_{1-6} alkyl group or an aryl group optionally having substituents, $-C(R^{9''})(R^{10''})-$ wherein $R^{9''}$ and $R^{10''}$ are the same or different and each is a hydrogen atom, a hydroxyl group, an amino group, a C_{1-6} alkyl group, a C_{1-6} hydroxyalkyl group or a C_{2-7} alkoxycarbonylamino group, or $R^{9''}$ and $R^{10''}$ may form, together with the adjacent carbon atom, a C_{3-7} cycloalkyl group, $-(CH_2)_m-NH-$ wherein m are as defined in the compound (1) of the present invention, $-CO-$ or a single bond; and

B is


(a'')


(b1'')


(b2'')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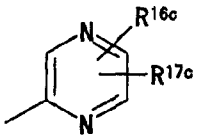
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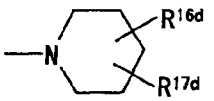
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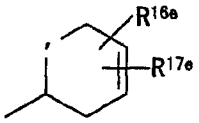
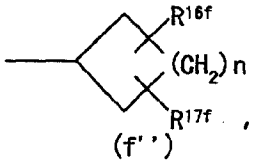
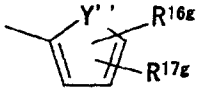
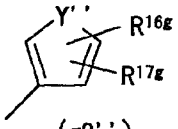
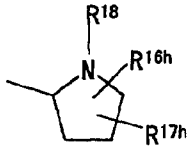

(e'')


(f'')


(g1'')


(g2'')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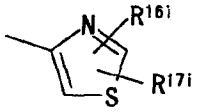
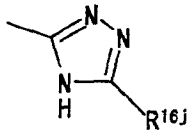

(i'')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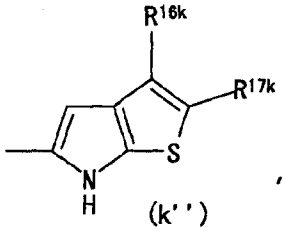
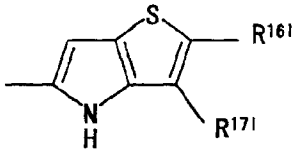
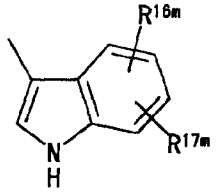
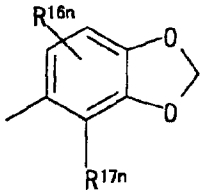

(k'')


(l'')


(m'')

or


(n'')

wherein $R^{11''}$, $R^{12''}$, $R^{13''}$, $R^{14''}$ and $R^{15''}$ are the same or different and each is a hydrogen atom, a halogen atom, a C_{1-6} alkyl group, a C_{1-6} alkoxy group, a nitro group, a hydroxyl group, a cyano group, a haloalkyl group, an aralkyl group, an aryl group optionally having substituents, an aryloxy group, a

tetrazolyl group, a triazolyl group, $-(CH_2)_p-CO-R^{19}$ wherein p and R^{19} are as defined in the compound (1) of the present invention, $-O-(CH_2)_r-R^{23}$ wherein r and R^{23} are as defined in the compound (1) of the present invention, $-O-CO-R^{27}$ wherein R^{27} is as defined in the compound (1) of the present invention or $-N(R^{28''})(R^{29''})$ wherein $R^{28''}$ and $R^{29''}$ are the same or different and each is a hydrogen atom, a C_{1-6} alkyl group, an aryl group optionally having substituents, $-(CH_2)_{p'}-COO-R^{30''}$ wherein p' is as defined for p and $R^{30''}$ is a hydrogen atom or a C_{1-6} alkyl group wherein the C_{1-6} alkyl group is optionally substituted by a hydroxyl group, a trifluoromethyl group or a carboxyl group, $-CON(R^{31})(R^{32})$ wherein R^{31} and R^{32} are as defined in the compound (1) of the present invention, $-CO-R^{33}$ wherein R^{33} is as defined in the compound (1) of the present invention or $-CO-(CH_2)_{r'}-R^{34}$ wherein r' and R^{34} are as defined in the compound (1) of the present invention,

$R^{16b}-R^{16n}$ and $R^{17b}-R^{17n}$ are as defined in the compound (1) of the present invention,

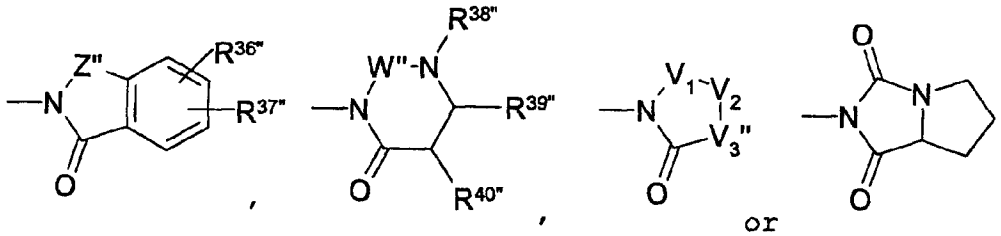
R^{18} is as defined in the compound (1) of the present invention,

Y'' is -S- or $-N(R^{35})-$ wherein R^{35} is as defined in the compound (1) of the present invention, and

n is as defined in the compound (1) of the present invention,

or

R^6 and R^7 may form, together with the adjacent nitrogen atom,



(i") , (ii") , (iii") or (iv)

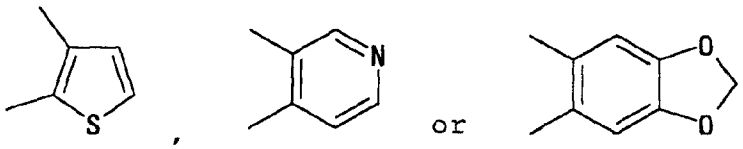
wherein $R^{36''}$ and $R^{37''}$ are the same or different and each is a hydrogen atom, a halogen atom, a C_{1-6} alkyl group, a C_{1-6} alkoxy group, an amino group, a hydroxyl group or $-O-CO-R^{41}$ wherein R^{41}

is as defined in the compound (1) of the present invention;

Z'' is $-CH_2-CH_2-$, $-C(R^{42})=CH-$, $-N=N-$, $-CO-$, $-CO-O-$, $-CO-CH_2-O-$, $-CH_2-CO-NH-$, $-C(R^{42''})(R^{43})-N(R^{44''})-$ wherein R^{42}, $R^{42''}$ and R^{43} are as defined in the compound (1) of the present invention and $R^{44''}$ is a hydrogen atom, a C_{1-6} alkyl group or a C_{2-7} alkoxycarbonyl group or $-C(U)-N(R^{44'''})-$ wherein U is =O or =S and $R^{44'''}$ is as defined for $R^{44''}$;

$R^{38''}$ is a hydrogen atom or an aryl group optionally having substituents;

$R^{39''}$ and $R^{40''}$ are the same or different and each is a hydrogen atom, a C_{1-6} alkyl group or a C_{2-7} alkoxycarbonyl group, or $R^{39''}$ and $R^{40''}$ may form, together with the adjacent carbon atom,



or

W'' is $-CO-$ or $-CH_2-$;

V_1 and V_2 are as defined in the compound (1) of the present invention; and

V_3'' is $-CH(R^{46''})-$ or $-N(R^{46'''})-$ wherein $R^{46''}$ and $R^{46'''}$ are the same or different and each is a hydrogen atom or an aryl group optionally having substituents.

Now, various substituents or positions of substitution are described in more detail in the following.

For R^1, it is preferably a hydrogen atom.

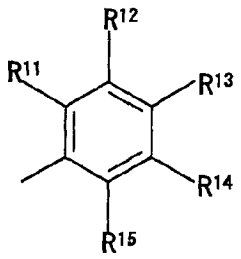
For R^2, it is preferably a hydrogen atom.

For R^3, it is preferably a C_{1-6} alkyl group or a halogen atom, particularly preferably a chlorine atom.

For R^4, it is preferably a hydrogen atom.

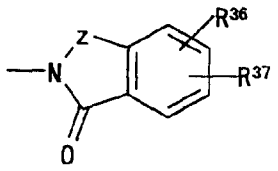
For R^5, it is preferably a hydrogen atom.

For R^7, X is preferably =O or -NH, A is a single bond and B forms



wherein each symbol is as defined above.

For R^6, it is preferably a hydrogen atom, or R^6 and R^7 may form, together with the adjacent nitrogen atom,



wherein each symbol is as defined above.

Preferable specific examples of the compound (1) of the present invention are shown in the following.

1-1. benzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-2. 2-aminobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-3. 2-hydroxybenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-4. 3-(2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenylcarbamoyloxy)-2,2-dimethylpropionic acid,

1-5. benzoic acid 2-(5-chloro-1H-indole-2-carbonyl)-1-methylhydrazide,

1-6. benzoic acid 2-(1-acetyl-5-chloro-1H-indole-2-carbonyl)hydrazide,

1-7. 5-chloro-1H-indole-2-carboxylic acid 2-(imino-phenyl-methyl)hydrazide,

1-8. 5-aminothiazole-4-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-9. benzoic acid 2-(5-fluoro-1H-indole-2-carbonyl)hydrazide,

1-10. cyclohexanecarboxylic acid 2-(5-fluoro-1H-indole-2-carbonyl)hydrazide,

1-11. thiophene-2-carboxylic acid 2-(5-fluoro-1H-indole-2-carbonyl)hydrazide,

1-12. 4-nitrobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-13. 2-methylbenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-14. 4-methylbenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-15. 2-methoxybenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-16. 3-methoxybenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-17. 4-methoxybenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-18. 3-methylbenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-19. 2-chlorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-20. 3-chlorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-21. 4-chlorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-22. 4-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)benzoic acid methyl ester,

1-23. cyclohexanecarboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-24. 2,4-dichlorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-25. 2,6-dichlorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-26. 2,4-difluorobenzoic acid 2-(5-chloro-1H-indole-2-

carbonyl)hydrazide,

1-27.biphenyl-2-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-28.3-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-29.4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-30.3-trifluoromethylbenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-31.4-trifluoromethylbenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-32.2-trifluoromethylbenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-33.benzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide,

1-34.benzoic acid 2-(5-chloro-3-methyl-1H-indole-2-carbonyl)hydrazide,

1-35.benzoic acid 2-(5,7-dichloro-1H-indole-2-carbonyl)hydrazide,

1-36.2-aminobenzoic acid 2-(5-isopropyl-1H-indole-2-carbonyl)hydrazide,

1-37.2-amino-4-fluorobenzoic acid 2-(5-isopropyl-1H-indole-2-carbonyl)hydrazide,

1-38.2-aminobenzoic acid 2-(5-fluoro-1H-indole-2-carbonyl)hydrazide,

1-39.2-aminobenzoic acid 2-(6-chloro-1H-indole-2-carbonyl)hydrazide,

1-40.3-amino-4-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)benzoic acid methyl ester,

1-41.3-aminoisonicotinic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-42.isonicotinic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-43.nicotinic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-44. pyridine-2-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-45. 3-(dimethylamino)benzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-46. N-(3-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenyl)acetamide,

1-47. N-(2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenyl)acetamide,

1-48. 4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)-2-methylhydrazide,

1-49. 2-(2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenoxy)acetic acid methyl ester,

1-50. 2-(2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenoxy)acetic acid,

1-51. 2-(dimethylamino)benzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-52. 2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenoxy-N,N-dimethylacetamide,

1-53. 2-methylaminobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-54. 2-amino-4-chlorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-55. 2-amino-6-chlorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-56. 2-amino-3-chlorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-57. 2-amino-5-chlorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-58. 4-cyanobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-59. 4-(1H-tetrazol-5-yl)benzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-60. 3-(1H-tetrazol-5-yl)benzoic acid 2-(5-chloro-1H-indole-2-

carbonyl)hydrazide,

1-61. 2-(2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)anilino)acetic acid,

1-62. 2-aminobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide,

1-63. 2-amino-4-fluorobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide,

1-64. methyl (2-(2-(5-methyl-1H-indole-2-carbonyl)hydrazinocarbonyl)phenyl)carbamate,

1-65. 2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenyl dimethylcarbamate,

1-66. 2-aminobenzoic acid 2-(5-ethyl-1H-indole-2-carbonyl)hydrazide,

1-67. 2-amino-4,5-difluorobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide,

1-68. 2-(2-hydroxyethoxy)benzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-69. 2-(3-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenoxy)acetic acid methyl ester,

1-70. 2-(3-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenoxy)acetic acid,

1-71. 2-(3-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenoxy)-N,N-dimethylacetamide,

1-72. 2-methylthiazole-4-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-73. 4-(2H-[1,2,4]triazol-3-yl)benzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-74. 3-(2H-[1,2,4]triazol-3-yl)benzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-75. 1,3-dihydroxy-2-propyl (2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenyl)carbamate,

1-76. 3-((2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenyl)carbamoyloxy)-2,2-

dimethylpropionic acid,

1-77. thiophene-2-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-78. furan-2-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-79. 2,6-dichloronicotinic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-80. 1H-pyrrole-2-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-81. 1H-imidazole-4-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-82. pyrazine-2-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-83. thiophene-3-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-84. furan-3-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-85. 5-chlorothiophene-2-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-86. 3-chlorothiophene-2-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-87. 1-methyl-1H-pyrrole-2-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-88. 5-methylthiophene-2-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-89. 3-methylthiophene-2-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-90. 2,6-difluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-91. 2,3-difluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-92. 5-chloro-1H-indole-2-carboxylic acid 2-(naphthalene-1-carbonyl)hydrazide,

1-93. 3,4,5-trifluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-94. 2,3,4,5-tetrafluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-95. 2-amino-4-methylbenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-96. 2-amino-4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-97. 2-amino-5-methylbenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-98. 2-amino-6-methylbenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-99. 2-amino-3-methylbenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-100. 2-amino-4,5-difluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-101. 3-aminothiophene-2-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-102. 2-aminobenzoic acid 2-(5-bromo-1H-indole-2-carbonyl)hydrazide,

1-103. 2-amino-4-fluorobenzoic acid 2-(5-bromo-1H-indole-2-carbonyl)hydrazide,

1-104. 1H-pyrazole-4-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-105. methyl (2-(2-(5-fluoro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenyl)carbamate,

1-106. 1-methyl-1H-pyrrole-2-carboxylic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide,

1-107. thiophene-3-carboxylic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide,

1-108. 4H-thieno[3,2-b]pyrrole-5-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-109. phenyl (2-(2-(5-chloro-1H-indole-2-

carbonyl)hydrazinocarbonyl)phenyl)carbamate,

1-110. benzyl (2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenyl)carbamate,

1-111. 2-hydroxyethyl (2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenyl)carbamate,

1-112. 3-hydroxypropyl (2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenyl)carbamate,

1-113. 2-((2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenyl)carbamoyloxy)acetic acid,

1-114. 2-((2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenyl)carbamoyloxymethyl)-2-methylmalonic acid,

1-115. methyl 2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenylcarbamate,

1-116. cyclohexanecarboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)-1-methylhydrazide,

1-117. thiophene-2-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)-1-methylhydrazide,

1-118. benzoic acid 2-(1H-indole-2-carbonyl)hydrazide,

1-119. benzoic acid 2-(5-chloro-1-methyl-1H-indole-2-carbonyl)hydrazide,

1-120. benzoic acid 2-(5-methoxy-1H-indole-2-carbonyl)hydrazide,

1-121. benzoic acid 2-(5-isopropyl-1H-indole-2-carbonyl)hydrazide,

1-122. benzoic acid 2-(5-nitro-1H-indole-2-carbonyl)hydrazide,

1-123. benzoic acid 2-(5-benzyloxy-1H-indole-2-carbonyl)hydrazide,

1-124. benzoic acid 2-(6-chloro-1H-indole-2-carbonyl)hydrazide,

1-125. 6H-thieno[2,3-b]pyrrole-5-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-126. 5-chloro-1H-indole-2-carboxylic acid 2-((2-fluorophenyl)-imino-methyl)hydrazide,

1-127. 5-chloro-1H-indole-2-carboxylic acid 2-((3-fluorophenyl)-imino-methyl)hydrazide,

1-128. 5-chloro-1H-indole-2-carboxylic acid 2-((4-fluorophenyl)-imino-methyl)hydrazide,

1-129. 5-chloro-1H-indole-2-carboxylic acid 2-(imino-(p-tolyl)-methyl)hydrazide,

1-130. 5-chloro-1H-indole-2-carboxylic acid 2-((4-chlorophenyl)-imino-methyl)hydrazide,

1-131. 5-chloro-1H-indole-2-carboxylic acid 2-((3-chlorophenyl)-imino-methyl)hydrazide,

1-132. 5-chloro-1H-indole-2-carboxylic acid 2-((3-fluorophenyl)-imino-methyl)hydrazide,

1-133. 5-chloro-1H-indole-2-carboxylic acid 2-(imino-(o-tolyl)-methyl)hydrazide,

1-134. 5-chloro-1H-indole-2-carboxylic acid 2-(imino-(m-tolyl)-methyl)hydrazide,

1-135. 5-chloro-1H-indole-2-carboxylic acid 2-(imino-(thiophen-2-yl)-methyl)hydrazide,

1-136. 5-chloro-1H-indole-2-carboxylic acid 2-(imino-(pyridin-2-yl)-methyl)hydrazide,

1-137. 5-chloro-1H-indole-2-carboxylic acid 2-((furan-2-yl)-imino-methyl)hydrazide,

1-138. 5-chloro-1H-indole-2-carboxylic acid 2-((2-chloro-6-fluorophenyl)-imino-methyl)hydrazide,

1-139. 5-chloro-1H-indole-2-carboxylic acid 2-(imino-(2-trifluoromethylphenyl)-methyl)hydrazide,

1-140. 5-chloro-1H-indole-2-carboxylic acid 2-(imino-(pyrazin-2-yl)-methyl)hydrazide,

1-141. 3-aminobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

1-142. 3-methoxybenzoic acid 2-(5-chloro-1H-indole-2-

carbonyl)hydrazide,

1-143. 5-amino-2-methylthiazole-4-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide,

2-1. 5-chloro-1H-indole-2-carboxylic acid (1,2,3,4-tetrahydro-2,4-dioxoquinazolin-3-yl)amide,

2-2. 5-chloro-1H-indole-2-carboxylic acid (2,3-dihydro-2,4-dioxo-4H-benzo[e][1,3]oxazin-3-yl)amide,

2-3. 5-chloro-1H-indole-2-carboxylic acid (1,2,3,4-tetrahydro-4-oxo-2-thioxoquinazolin-3-yl)amide,

2-4. 5-chloro-1H-indole-2-carboxylic acid (3,4-dihydro-2-methyl-4-oxoquinazolin-3-yl)amide,

2-5. 5-chloro-1H-indole-2-carboxylic acid (3,4-dihydro-4-oxoquinazolin-3-yl)amide,

2-6. 5-chloro-1H-indole-2-carboxylic acid (1,2,3,4-tetrahydro-4-oxoquinazolin-3-yl)amide,

2-7. 5-chloro-1H-indole-2-carboxylic acid (1,2,3,4-tetrahydro-2,5-dioxo-5H-benzo[e][1,4]diazepin-4-yl)amide,

2-8. 5-chloro-1H-indole-2-carboxylic acid (2,3,4,5-tetrahydro-3,5-dioxo-benzo[f][1,4]oxazepin-4-yl)amide,

2-9. 5-isopropyl-1H-indole-2-carboxylic acid (1,2,3,4-tetrahydro-2,4-dioxoquinazolin-3-yl)amide,

2-10. 5-isopropyl-1H-indole-2-carboxylic acid (7-fluoro-1,2,3,4-tetrahydro-2,4-dioxoquinazolin-3-yl)amide,

2-11. 5-fluoro-1H-indole-2-carboxylic acid (1,2,3,4-tetrahydro-2,4-dioxoquinazolin-3-yl)amide,

2-12. 6-chloro-1H-indole-2-carboxylic acid (1,2,3,4-tetrahydro-2,4-dioxoquinazolin-3-yl)amide,

2-13. 3-((5-chloro-1H-indole-2-carbonyl)amino)-1,2,3,4-tetrahydro-2,4-dioxoquinazoline-7-carboxylic acid methyl ester,

2-14. 3-((5-chloro-1H-indole-2-carbonyl)amino)-1,2,3,4-tetrahydro-2,4-dioxoquinazoline-7-carboxylic acid,

2-15. 5-chloro-1H-indole-2-carboxylic acid (1,2,3,4-tetrahydro-

2,4-dioxo-6-(trifluoroacetylamino)quinazolin-3-yl)amide,

2-16. 5-chloro-1H-indole-2-carboxylic acid (6-amino-1,2,3,4-tetrahydro-2,4-dioxoquinazolin-3-yl)amide,

2-17. 5-chloro-1H-indole-2-carboxylic acid (5-chloro-1,2,3,4-tetrahydro-2,4-dioxoquinazolin-3-yl)amide,

2-18. 5-chloro-1H-indole-2-carboxylic acid (6-chloro-1,2,3,4-tetrahydro-2,4-dioxoquinazolin-3-yl)amide,

2-19. 5-chloro-1H-indole-2-carboxylic acid (7-chloro-1,2,3,4-tetrahydro-2,4-dioxoquinazolin-3-yl)amide,

2-20. 5-chloro-1H-indole-2-carboxylic acid (8-chloro-1,2,3,4-tetrahydro-2,4-dioxoquinazolin-3-yl)amide,

2-21. 2-(3-((5-chloro-1H-indole-2-carbonyl)amino)-1,2,3,4-tetrahydro-2,4-dioxoquinazolin-1-yl)acetic acid,

2-22. 2-(3-((5-chloro-1H-indole-2-carbonyl)amino)-1,2,3,4-tetrahydro-2,4-dioxoquinazolin-1-yl)acetic acid methyl ester,

2-23. 5-methyl-1H-indole-2-carboxylic acid (1,2,3,4-tetrahydro-2,4-dioxoquinazolin-3-yl)amide,

2-24. 5-methyl-1H-indole-2-carboxylic acid (7-fluoro-1,2,3,4-tetrahydro-2,4-dioxoquinazolin-3-yl)amide,

2-25. 5-ethyl-1H-indole-2-carboxylic acid (1,2,3,4-tetrahydro-2,4-dioxoquinazolin-3-yl)amide,

2-26. 5-methyl-1H-indole-2-carboxylic acid (6,7-difluoro-1,2,3,4-tetrahydro-2,4-dioxoquinazolin-3-yl)amide,

2-27. 5-methyl-1H-indole-2-carboxylic acid (1,2,3,4-tetrahydro-6-methoxy-2,4-dioxoquinazolin-3-yl)amide,

2-28. 5-methyl-1H-indole-2-carboxylic acid (1,2,3,4-tetrahydro-6-hydroxy-2,4-dioxoquinazolin-3-yl)amide,

2-29. acetic acid 3-((5-methyl-1H-indole-2-carbonyl)amino)-1,2,3,4-tetrahydro-2,4-dioxoquinazolin-6-yl ester,

2-30. 5-chloro-1H-indole-2-carboxylic acid (1,2,3,4-tetrahydro-2,4-dioxo-1-propylquinazolin-3-yl)amide,

2-31. 5-chloro-1H-indole-2-carboxylic acid (1,2,3,4-tetrahydro-1-methyl-2,4-dioxoquinazolin-3-yl)amide,

2-32. N-(1,2,3,4-tetrahydro-7-nitro-2,4-dioxoquinazolin-3-yl)-5-chloro-1H-indole-2-carboxylic acid amide,

3-1. 5-chloro-1H-indole-2-carboxylic acid (2,4-dioxoperhydropyrimidin-3-yl)amide,

3-2. 5-chloro-1H-indole-2-carboxylic acid (4-oxo-2-thioxoperhydropyrimidin-3-yl)amide,

3-3. 5-chloro-1H-indole-2-carboxylic acid (2,4-dioxo-1-phenylperhydropyrimidin-3-yl)amide,

3-4. 5-chloro-1H-indole-2-carboxylic acid (4-oxo-1-phenylperhydropyrimidin-3-yl)amide,

3-5. 5-chloro-1H-indole-2-carboxylic acid (1-(4-fluorophenyl)-2,4-dioxoperhydropyrimidin-3-yl)amide,

3-6. 5-chloro-1H-indole-2-carboxylic acid (2,4-dioxo-1-(pyridin-2-yl)perhydropyrimidin-3-yl)amide,

3-7. 5-chloro-1H-indole-2-carboxylic acid (1-(3-fluorophenyl)-2,4-dioxoperhydropyrimidin-3-yl)amide,

3-8. 5-chloro-1H-indole-2-carboxylic acid (1-(2-fluorophenyl)-2,4-dioxoperhydropyrimidin-3-yl)amide,

3-9. 5-fluoro-1H-indole-2-carboxylic acid (2,4-dioxo-1-phenyl-perhydropyrimidin-3-yl)amide,

3-10. 5-methyl-1H-indole-2-carboxylic acid (2,4-dioxo-1-phenyl-perhydropyrimidin-3-yl)amide,

3-11. 5-chloro-1H-indole-2-carboxylic acid (1-(3-chlorophenyl)-2,4-dioxoperhydropyrimidin-3-yl)amide,

3-12. 5-chloro-1H-indole-2-carboxylic acid (2,4-dioxo-1-(m-tolyl)perhydropyrimidin-3-yl)amide,

3-13. 5-chloro-1H-indole-2-carboxylic acid (2,4-dioxo-1-(p-tolyl)perhydropyrimidin-3-yl)amide,

3-14. 5-chloro-1H-indole-2-carboxylic acid (1-(4-chlorophenyl)-2,4-dioxoperhydropyrimidin-3-yl)amide,

3-15. 5-chloro-1H-indole-2-carboxylic acid (2,4-dioxo-1-(o-tolyl)perhydropyrimidin-3-yl)amide,

4-1. 5-chloro-1H-indole-2-carboxylic acid ((4S)-2,5-dioxo-4-

phenylimidazolidin-1-yl)amide,

4-2. 5-chloro-1H-indole-2-carboxylic acid (2,4-dioxo-1-phenylimidazolidin-3-yl)amide,

4-3. 5-chloro-1H-indole-2-carboxylic acid (4-oxo-1-phenyl-2-thioxoimidazolidin-3-yl)amide,

4-4. 5-chloro-1H-indole-2-carboxylic acid (4-oxo-1-phenylimidazolidin-3-yl)amide,

4-5. 5-chloro-1H-indole-2-carboxylic acid (2-oxo-1-phenylimidazolidin-3-yl)amide,

4-6. 5-chloro-1H-indole-2-carboxylic acid ((4R)-2,5-dioxo-4-phenylimidazolidin-1-yl)amide,

4-7. 5-chloro-1H-indole-2-carboxylic acid ((4S)-1,3-dioxo-perhydropyrrolo[1,2-c]imidazol-2-yl)amide,

4-8. 5-chloro-1H-indole-2-carboxylic acid ((4R)-1,3-dioxo-perhydropyrrolo[1,2-c]imidazol-2-yl)amide,

4-9. 5-chloro-1H-indole-2-carboxylic acid ((4S)-4-benzyl-2,5-dioxoimidazolidin-1-yl)amide,

4-10. 5-chloro-1H-indole-2-carboxylic acid ((4R)-4-benzyl-2,5-dioxoimidazolidin-1-yl)amide,

4-11. 5-chloro-1H-indole-2-carboxylic acid (2,4-dioxoimidazolidin-3-yl)amide,

4-12. 5-chloro-1H-indole-2-carboxylic acid (1-methyl-2,5-dioxo-4-phenylimidazolidin-1-yl)amide,

4-13. 5-chloro-1H-indole-2-carboxylic acid (2,4-dioxo-1-(4-fluorophenyl)imidazolidin-3-yl)amide,

4-14. 5-chloro-1H-indole-2-carboxylic acid (2,5-dioxo-4-(2-fluorophenyl)imidazolidin-1-yl)amide,

4-15. 5-chloro-1H-indole-2-carboxylic acid (2,5-dioxo-4-(2-thienyl)imidazolidin-1-yl)amide,

4-16. 5-chloro-1H-indole-2-carboxylic acid (2,5-dioxo-4-(4-fluorophenyl)imidazolidin-1-yl)amide,

4-17. 5-chloro-1H-indole-2-carboxylic acid (2,5-dioxo-4-(4-chlorophenyl)imidazolidin-1-yl)amide,

4-18. 5-chloro-1H-indole-2-carboxylic acid ((4S)-2,5-dioxo-4-(4-hydroxyphenyl)imidazolidin-1-yl)amide,

4-19. 5-chloro-1H-indole-2-carboxylic acid ((4S)-2,5-dioxo-4-(4-methoxyphenyl)imidazolidin-1-yl)amide,

4-20. 5-chloro-1H-indole-2-carboxylic acid ((4R)-2,5-dioxo-4-(4-methoxyphenyl)imidazolidin-1-yl)amide,

5-1. 5-chloro-1H-indole-2-carboxylic acid 2-(anilinocarbonyl)hydrazide,

5-2. 5-chloro-1H-indole-2-carboxylic acid 2-(phenylthiocarbonyl)hydrazide,

5-3. 5-chloro-1H-indole-2-carboxylic acid 2-(2-phenylacetyl)hydrazide,

5-4. 5-chloro-1H-indole-2-carboxylic acid 2-(2-oxo-2-phenylacetyl)hydrazide,

5-5. 5-chloro-1H-indole-2-carboxylic acid 2-((2-fluorophenyl)aminocarbonyl)hydrazide,

5-6. 5-chloro-1H-indole-2-carboxylic acid 2-((3-fluorophenyl)aminocarbonyl)hydrazide,

5-7. 5-chloro-1H-indole-2-carboxylic acid 2-((4-fluorophenyl)aminocarbonyl)hydrazide,

5-8. 5-chloro-1H-indole-2-carboxylic acid 2-(anilinocarbonyl)-2-methylhydrazide,

5-9. 5-chloro-1H-indole-2-carboxylic acid 2-((2-chloroanilino)carbonyl)hydrazide,

5-10. 5-chloro-1H-indole-2-carboxylic acid 2-((3-chloroanilino)carbonyl)hydrazide,

5-11. 5-chloro-1H-indole-2-carboxylic acid 2-((4-chloroanilino)carbonyl)hydrazide,

5-12. 5-chloro-1H-indole-2-carboxylic acid 2-((1-phenylcyclopropane)carbonyl)hydrazide,

5-13. 5-chloro-1H-indole-2-carboxylic acid 2-((1-phenylcyclopentane)carbonyl)hydrazide,

5-14. 5-chloro-1H-indole-2-carboxylic acid 2-((1-

phenylcyclohexane)carbonyl)hydrazide,

5-15. 5-chloro-1H-indole-2-carboxylic acid 2-(2-phenylpropanoyl)hydrazide,

5-16. 5-chloro-1H-indole-2-carboxylic acid 2-(3-hydroxy-2-phenylpropanoyl)hydrazide,

5-17. 5-chloro-1H-indole-2-carboxylic acid 2-(2-methyl-2-phenylpropanoyl)hydrazide,

5-18. 5-chloro-1H-indole-2-carboxylic acid 2-((2S)-2-amino-2-phenylacetyl)hydrazide,

5-19. N-(2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazino)-2-oxo-1-phenylethyl)acetamide,

6-1. 2-morpholinoethyl (2-((2-(5-chloro-1H-indole-2-carbonyl)hydrazino)carbonyl)phenyl)carbamate p-toluenesulfonate,

6-2. 2-amino-4,5-difluorobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide benzenesulfonate,

6-3. 2-amino-4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide benzenesulfonate,

6-4. 3-(dimethylamino)benzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide methanesulfonate,

6-5. 2-amino-4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide hydrochloride,

6-6. 2-amino-4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide p-toluenesulfonate,

6-7. 2-amino-4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide p-toluenesulfonate,

6-8. 2-amino-4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide p-toluenesulfonate,

6-9. 2-amino-4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide p-toluenesulfonate,

6-10. 2-aminobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide p-toluenesulfonate,

6-11. 2-aminobenzoic acid 2-(5-methyl-1H-indole-2-

carbonyl)hydrazide benzenesulfonate,

6-12. 2-amino-4-fluorobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide benzenesulfonate,

6-13. 3-aminobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide p-toluenesulfonate,

6-14. 5-chloro-1H-indole-2-carboxylic acid 2-((2-chlorophenyl)-imino-methyl)hydrazide methanesulfonate,

6-15. 5-chloro-1H-indole-2-carboxylic acid 2-((2-chlorophenyl)-imino-methyl)hydrazide p-toluenesulfonate,

6-16. 5-chloro-1H-indole-2-carboxylic acid 2-((2-chlorophenyl)-imino-methyl)hydrazide hydrochloride,

6-17. 5-chloro-1H-indole-2-carboxylic acid 2-(imino-phenyl-methyl)hydrazide methanesulfonate,

6-18. 5-chloro-1H-indole-2-carboxylic acid 2-((2-chlorophenyl)-imino-methyl)hydrazide butenedioic acid salt,

6-19. 5-chloro-1H-indole-2-carboxylic acid 2-((2-fluorophenyl)-imino-methyl)hydrazide hydrochloride,

6-20. 5-chloro-1H-indole-2-carboxylic acid 2-((2-fluorophenyl)-imino-methyl)hydrazide methanesulfonate,

6-21. 5-chloro-1H-indole-2-carboxylic acid 2-((1-imino-2-phenylethyl)hydrazide methanesulfonate,

6-22. 5-chloro-1H-indole-2-carboxylic acid 2-((3-fluorophenyl)-imino-methyl)hydrazide hydrochloride,

6-23. 5-chloro-1H-indole-2-carboxylic acid 2-((3,4-difluorophenyl)-imino-methyl)hydrazide methanesulfonate,

6-24. 5-chloro-1H-indole-2-carboxylic acid 2-(imino-(2-methoxyphenyl)-methyl)hydrazide methanesulfonate,

6-25. 5-chloro-1H-indole-2-carboxylic acid 2-((2,6-difluorophenyl)-imino-methyl)hydrazide methanesulfonate,

6-26. 5-chloro-1H-indole-2-carboxylic acid 2-((2,4-difluorophenyl)-imino-methyl)hydrazide methanesulfonate,

6-27. 5-chloro-1H-indole-2-carboxylic acid 2-((1,2-dimethyl-1H-pyrrol-5-yl)-imino-methyl)hydrazide methanesulfonate,

6-28. 2-aminobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide p-toluenesulfonate,

6-29. 2-aminobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide benzenesulfonate,

6-30. 2-amino-4-fluorobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide benzenesulfonate,

6-31. 2-(dimethylamino)benzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide p-toluenesulfonate,

6-32. 2-amino-4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide methanesulfonate,

6-33. 2-aminobenzoic acid 2-(5-bromo-1H-indole-2-carbonyl)hydrazide methanesulfonate,

6-34. 2-amino-4-fluorobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide p-toluenesulfonate, and

6-35. 2-amino-4-fluorobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide methanesulfonate.

The number placed on the left end corresponds to Example No. (1-1, 2-1, 3-1, 4-1, 5-1 and 6-1 correspond to Example 1, 2, 3, 4, 5 and 6, respectively). Of these, preferred are the compounds of the above-mentioned 1-1 - 1-143 and 6-1 - 6-35, and more preferred are the compounds of the above-mentioned 6-1 - 6-35.

Here, the compound (1) of the present invention may be a hydrate or a solvate, and encompasses a prodrug thereof and a metabolite thereof.

A "prodrug" of a compound is a derivative of the compound (1) of the present invention, which has a chemically or metabolically decomposable group, and is decomposed by hydrolysis or solvolysis, or under physiological conditions to show pharmaceutical activity. For example, a compound wherein a hydroxyl group is substituted by -CO-alkyl, -CO_2-alkyl, -CONH-alkyl, -CO-alkenyl, -CO_2-alkenyl, -CONH-alkenyl, -CO-aryl, -CO_2-aryl, -CONH-aryl, -CO-heterocycle, -CO_2-heterocycle, -

CONH-heterocycle wherein alkyl, alkenyl, aryl and heterocycle are optionally substituted by halogen atom, alkyl group, hydroxyl group, alkoxy group, carboxy group, amino group, amino acid residue, $-PO_3H_2$, $-SO_3H$, $-OPO_3H_2$, $-OSO_3H$ and the like, -CO-polyethylene glycol residue, $-CO_2$-polyethylene glycol residue, -CO-polyethylene glycol monoalkyl ether residue, $-CO_2$-polyethylene glycol monoalkyl ether residue, $-PO_3H_2$ and the like,

a compound wherein an amino group is substituted by -CO-alkyl, $-CO_2$-alkyl, -CO-alkenyl, $-CO_2$-alkenyl, $-CO_2$-aryl, -CO-aryl, -CO-heterocycle, $-CO_2$-heterocycle wherein alkyl, alkenyl, aryl and heterocycle are optionally substituted by halogen atom, alkyl group, hydroxyl group, alkoxy group, carboxy group, amino group, amino acid residue, $-PO_3H_2$, $-SO_3H$, $-OPO_3H_2$, $-OSO_3H$ and the like, -CO-polyethylene glycol residue, $-CO_2$-polyethylene glycol residue, -CO-polyethylene glycol monoalkyl ether residue, $-CO_2$-polyethylene glycol monoalkyl ether residue, $-PO_3H_2$ and the like, and

a compound wherein a carboxy group is substituted by alkoxy group, aryloxy group wherein alkoxy group and aryloxy group are optionally substituted by halogen atom, alkyl group, hydroxyl group, alkoxy group, carboxy group, amino group, amino acid residue, $-PO_3H_2$, $-SO_3H$, $-OPO_3H_2$, $-OSO_3H$ and the like, polyethylene glycol residue, polyethylene glycol monoalkyl ether residue and the like can be mentioned.

When the compound of the present invention is to be used as a therapeutic agent for diabetes, it is administered systemically or topically, and orally or parenterally. The dose varies depending on the age, body weight, symptom, treatment effect and the like, but it is generally administered in the range of 10 mg to 1 g per dose for an adult once to several times a day.

To give a preparation of a solid composition and liquid

composition for oral administration or injectable solution and the like for parenteral administration, the compound (1) of the present invention can be mixed with a suitable diluent, dispersant, adsorbent, solubilizer and the like.

The compound (1) of the present invention can be used for the treatment or prophylaxis of diabetes in human as well as animals besides human, such as mammals.

The compound (1) of the present invention can be used together with one or more other pharmaceutical agents by a conventional method generally used for pharmaceutical agents. While there are various pharmaceutical agents that can be used together with the compound (1) of the present invention, therapeutic agents for hyperlipidemia and therapeutic agents for diabetes are particularly preferable.

As the therapeutic agents for hyperlipidemia that can be used concurrently, statin agents can be mentioned, which are specifically lovastatin, simvastatin, pravastatin, fluvastatin, atorvastatin, cerivastatin and the like.

Similarly, as the therapeutic agents for diabetes that can be used concurrently, insulin preparations, sulfonylurea agents, insulin secretagogues, sulfonamides, biguanides, α-glucosidase inhibitors, insulin sensitizers and the like can be mentioned, which are as follows. As the insulin preparation, for example, insulin and the like, as the sulfonylurea agent, glibenclamide, torbutamide, glyclopyramide, acetohexamide, glimepiride, tolazamide, gliclazide, nateglinide and the like, as the sulfonamide, glybuzole and the like, as the biguanide, metformin hydrochloride, buformin hydrochloride and the like, as the α-glucosidase inhibitor, voglibose, acarbose and the like, and as the insulin sensitizer, pioglitazone hydrochloride and the like can be mentioned.

The present inventors have also found that a combined use with an HLGPa inhibitor that has not been used

concurrently with the therapeutic agents for diabetes affords a synergistic therapeutic or prophylaxis effect on diabetes, in comparison with a single use of each pharmaceutical agent. In other words, a combined use of the compound (1) of the present invention with a therapeutic agent for diabetes is useful from the aspect of effect.

Now, one example of the production method of an indole compound represented by compound (1) is shown below. However, the production method of the present invention is not limited to the example.

When the reaction to be mentioned below is conducted, functional groups other than the concerned moiety may be previously protected as necessary and deprotected at a suitable stage.

The amount of the solvent to be used for each step is not particularly limited as long as the reaction mixture can be stirred.

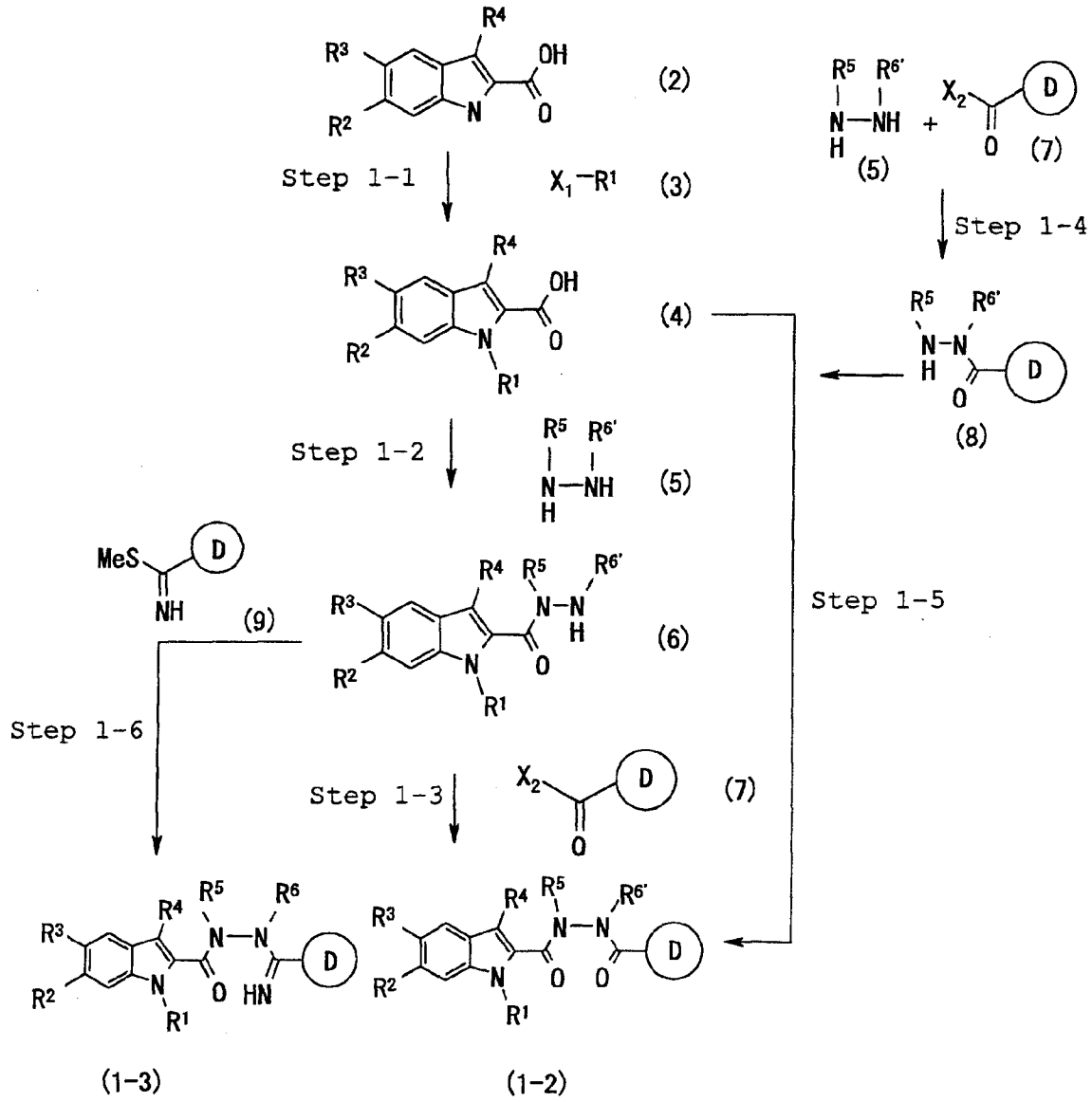
The reagent to be used for each step may be in the form of a hydrate thereof, a salt thereof and the like, as long as the objective reaction is not inhibited.

The reaction in each step may be carried out by a conventional method and for isolation and purification, conventional methods such as crystallization, recrystallization, column chromatography, preparative HPLC and the like are appropriately selected, or used in combination.

Production Method 1

A production method of a compound represented by the formula (1) wherein R^7 is $-C(=O)-D$ or $-C(=NH)-D$ wherein D is a group selected from the groups represented by the formulas (a)-(s) is exemplarily shown in the following.

Production Method



wherein R^1, R^2, R^3, R^4 and R^5 are as defined above, $R^{6'}$ is a hydrogen atom, a C_{1-6} alkyl group or an aralkyl group (aralkyl group is optionally substituted by a halogen atom), X_1 is a halogen atom, X_2 is a halogen atom or a hydroxyl group, and D (or also referred to as "ring D") is a group selected from the groups represented by the formulas (a)-(s).

Step 1-1

A compound represented by the formula (4) can be obtained by reacting a compound represented by the formula (2) with a

compound represented by the formula (3) in a solvent in the presence of a base.

As the base to be used in the reaction, for example, alkali metal hydrides such as sodium hydride, potassium hydride etc.; alkali metal alkoxides such as sodium ethoxide, sodium methoxide, potassium tert-butoxide etc.; alkyllithiums such as n-butyllithium, sec-butyllithium etc.; alkali metal azides such as lithium diisopropylamide, sodium amide, lithium bistrimethylsilylazide etc.; alkali metal carbonates such as sodium carbonate, potassium carbonate etc.; alkali metal hydrogen carbonate such as sodium hydrogen carbonate, potassium hydrogen carbonate etc.; alkali metal hydroxides such as lithium hydroxide, sodium hydroxide, potassium hydroxide etc.; alkali metal carboxylates such as sodium acetate, potassium acetate etc.; alkali metal phosphates such as sodium phosphate, potassium phosphate etc.; organic bases such as triethylamine, pyridine, N-methylmorpholine etc.; can be mentioned. Preferred is sodium hydride.

As the solvent, for example, ether solvents such as diethyl ether, tetrahydrofuran (THF), dioxane, 1,2-dimethoxyethane, diglyme etc.; hydrocarbon solvents such as benzene, toluene, hexane, xylene etc.; halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane etc.; alcohol solvents such as methanol, ethanol, isopropyl alcohol, tert-butanol etc.; ester solvents such as ethyl acetate, methyl acetate, butyl acetate etc.; polar solvents such as acetone, N,N-dimethylformamide, dimethyl sulfoxide etc.; and the like can be mentioned. These may be used alone or in combination. Preferable solvent for this reaction is N,N-dimethylformamide.

The reaction temperature is generally -50°C to 50°C, preferably -20°C to room temperature.

The reaction time is generally 1-10 hr, preferably 1-5 hr,

more preferably 2-5 hr.

Step 1-2

A compound represented by the formula (6) can be obtained by reacting a compound represented by the formula (4) with a compound represented by the formula (5) in a solvent in the presence of condensing agent.

As the solvent, for example, ether solvents such as diethyl ether, tetrahydrofuran, dioxane, 1,2-dimethoxyethane, diglyme etc.; hydrocarbon solvents such as benzene, toluene, hexane, xylene etc.; halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane etc.; alcohol solvents such as methanol, ethanol, isopropyl alcohol, tert-butanol etc.; ester solvents such as ethyl acetate, methyl acetate, butyl acetate etc.; polar solvent such as acetone, N,N-dimethylformamide, dimethyl sulfoxide etc.; and the like can be mentioned, These may be used alone or in combination. Preferable solvent for this reaction is N,N-dimethylformamide.

The condensing agent may be any as long as it is used for general methods of peptide condensation (e.g., acid chloride method, mixed acid anhydride method etc.). Of these, a combination of 1-hydroxybenzotriazole monohydrate and 1-(3-(dimethylamino)propyl)-3-ethylcarbodiimide hydrochloride is preferable.

The reaction temperature is generally -20°C to 50°C, preferably 0°C to room temperature.

The reaction time is generally 1-48 hr, preferably 2-24 hr.

Step 1-3

A compound represented by the formula (1-2), which is one of the object compounds, can be obtained by reacting a compound represented by the formula (6) with a compound represented by the formula (7) in a solvent by using a

condensing agent or a base. For smooth progress of this reaction, a base can be used. For example, for the formula (7) when X_2 is a hydroxyl group, a condensing agent is used, in which a base may be used for a smooth reaction. When X_2 is a halogen atom, moreover, the reaction can be carried out smoothly by the use of base, even if a condensing agent is not used.

As the solvent to be used in the reaction, for example, ether solvents such as diethyl ether, tetrahydrofuran, dioxane, 1,2-dimethoxyethane, diglyme etc.; hydrocarbon solvents such as benzene, toluene, hexane, xylene etc.; halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane etc.; alcohol solvents such as methanol, ethanol, isopropyl alcohol, tert-butanol etc.; ester solvents such as ethyl acetate, methyl acetate, butyl acetate etc.; polar solvents such as acetone, N,N-dimethylformamide, dimethyl sulfoxide etc.; and the like can be mentioned, These may be used alone or in combination. Preferable solvent for this reaction is N,N-dimethylformamide and THF.

The condensing agent may be any as long as it is used for general methods of peptide condensation (e.g., acid chloride method, mixed acid anhydride method etc.). Of these, a combination of 1-hydroxybenzotriazole monohydrate and 1-(3-(dimethylamino)propyl)-3-ethylcarbodiimide hydrochloride is preferable.

As the base, for example, organic bases such as triethylamine, N-methylmorpholine etc. and the like can be mentioned. Preferred is triethylamine.

The reaction temperature is generally -10°C to 60°C, preferably 0°C to room temperature.

The reaction time is generally not less than 10 min., preferably 1-24 hr, more preferably 3-15 hr, further preferably 3-12 hr.

Step 1-4

A compound represented by the formula (8) can be obtained by subjecting a compound represented by the formula (5) to condensation reaction with a compound represented by the formula (7) in a solvent using a condensing agent.

As the solvent, for example, ether solvents such as diethyl ether, tetrahydrofuran, dioxane, 1,2-dimethoxyethane, diglyme etc.; hydrocarbon solvents such as benzene, toluene, hexane, xylene etc.; halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane etc.; alcohol solvents such as methanol, ethanol, isopropyl alcohol, tert-butanol etc.; ester solvents such as ethyl acetate, methyl acetate, butyl acetate etc.; polar solvents such as acetone, N,N-dimethylformamide, dimethyl sulfoxide etc.; and the like can be mentioned, These may be used alone or in combination. Preferable solvent for this reaction is N,N-dimethylformamide.

The condensing agent may be any as long as it is used for general methods of peptide condensation (e.g., acid chloride method, mixed acid anhydride method etc.). Of these, a combination of 1-hydroxybenzotriazole monohydrate and 1-(3-(dimethylamino)propyl)-3-ethylcarbodiimide hydrochloride is preferable.

The reaction temperature is generally -30°C to 50°C, preferably -20°C to room temperature.

The reaction time is generally 1-48 hr, preferably 12-24 hr.

Step 1-5

A compound represented by the formula (1-2), which is one of the object compounds, can be obtained by subjecting a compound represented by the formula (8) to condensation reaction with a compound represented by the formula (4) in a solvent using a condensing agent.

As the solvent, for example, ether solvents such as diethyl ether, tetrahydrofuran, dioxane, 1,2-dimethoxyethane, diglyme etc.; hydrocarbon solvents such as benzene, toluene, hexane, xylene etc.; halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane etc.; alcohol solvents such as methanol, ethanol, isopropyl alcohol, tert-butanol etc.; ester solvents such as ethyl acetate, methyl acetate, butyl acetate etc.; polar solvents such as acetone, N,N-dimethylformamide, dimethyl sulfoxide etc.; and the like can be mentioned. These may be used alone or in combination. Preferable solvent for this reaction is N,N-dimethylformamide.

The condensing agent may be any as long as it is used for general methods of peptide condensation (e.g., acid chloride method, mixed acid anhydride method etc.). Of these, a combination of 1-hydroxybenzotriazole monohydrate and 1-(3-(dimethylamino)propyl)-3-ethylcarbodiimide hydrochloride is preferable.

The reaction temperature is generally -30°C to 50°C, preferably -20°C to room temperature.

The reaction time is generally 1-48 hr, preferably 1-24 hr.

Step 1-6

A compound represented by the formula (1-3), which is one of the object compounds, can be obtained by reacting a compound represented by the formula (6) with a compound represented by the formula (9) or a regent equivalent thereto (e.g., methyl benzimidate hydrochloride etc.) in a solvent.

As the solvent, for example, ether solvents such as diethyl ether, tetrahydrofuran, dioxane, 1,2-dimethoxyethane, diglyme etc.; hydrocarbon solvents such as benzene, toluene, hexane, xylene etc.; halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane etc.; alcohol solvents such as methanol, ethanol, isopropyl alcohol,

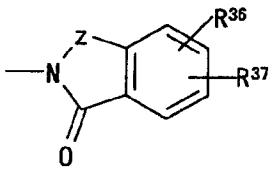
tert-butanol etc.; ester solvents such as ethyl acetate, methyl acetate, butyl acetate etc.; polar solvents such as acetone, N,N-dimethylformamide, dimethyl sulfoxide etc.; and the like can be mentioned, These may be used alone or in combination. Preferable solvent for this reaction is, methanol.

The reaction temperature is generally -30°C to 50°C, preferably 0°C to room temperature.

The reaction time is generally 3-48 hr, preferably 12-24 hr.

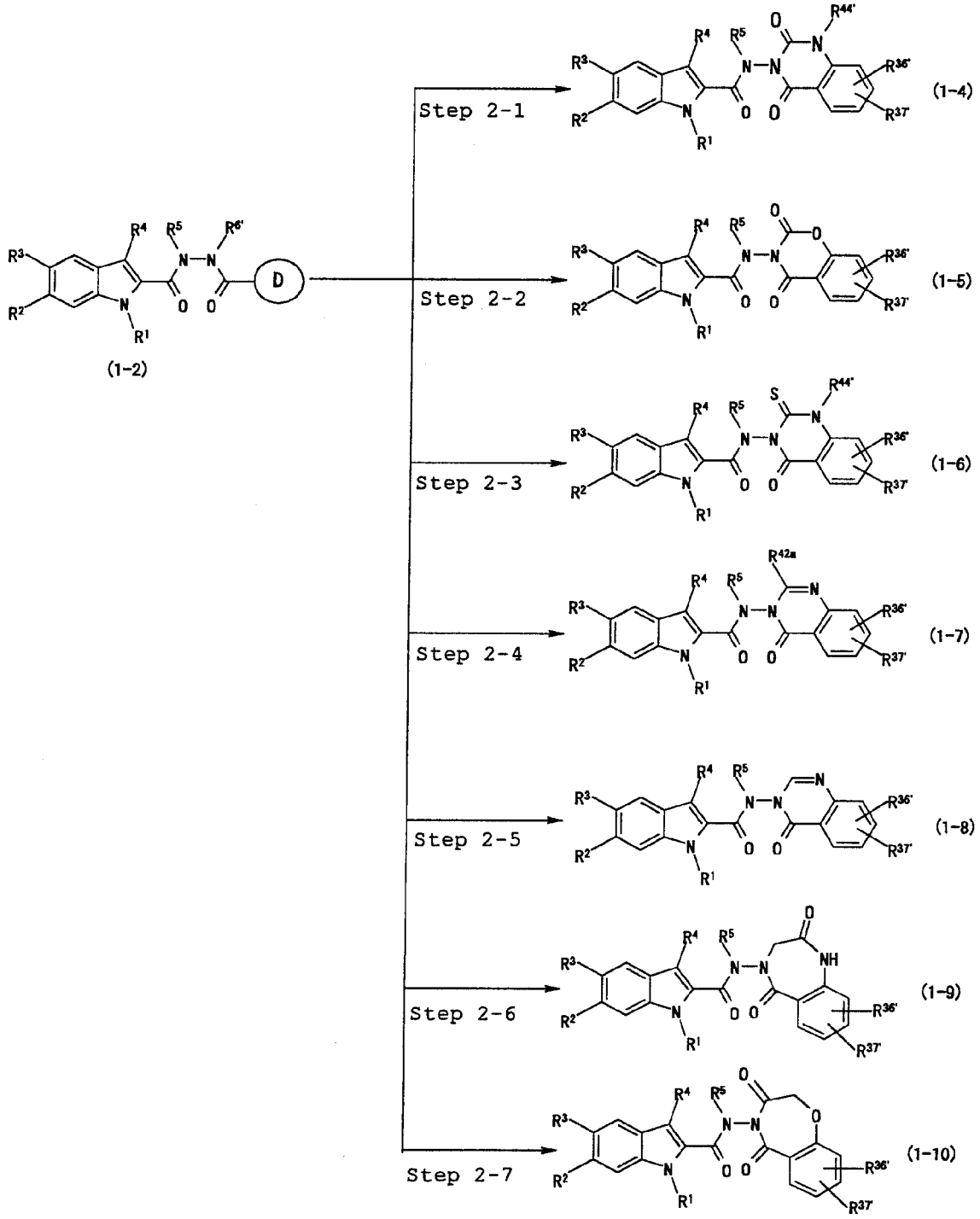
Production method 2

A compound represented by the formula (1), wherein R^6 and R^7 show, together with the nitrogen atom bonded thereto,



wherein Z, R^{36} and R^{37} are as defined above, is exemplarily shown in the following.

Production Method 2

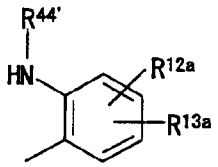


wherein R^1, R^2, R^3, R^4, R^5, $R^{44'}$ and ring D are as defined above, $R^{6'}$ is a hydrogen atom, a C_{1-6} alkyl group or an aralkyl group (aralkyl group is optionally substituted by a halogen atom), $R^{36'}$ and $R^{37'}$ are each a hydrogen atom, a halogen atom, a C_{1-6}

alkyl group, a C_{1-6} alkoxy group or a hydroxyl group, and R^{42a} is a C_{1-6} alkyl group).

Step 2-1

A compound represented by the formula (1-4), which is one of the object compounds, can be obtained by reacting a compound wherein ring D is



wherein R^{12a} and R^{13a} are the same or different and each is a hydrogen atom, a halogen atom, a C_{1-6} alkyl group, a C_{1-6} alkoxy group or a hydroxyl group (R^{12a} and R^{13a} are as defined for $R^{36'}$ and $R^{37'}$) and R^{44} is as defined above, from among the compounds represented by the formula (1-2) obtained in Steps 1-3 and 1-5, in a solvent, using a phosgene equivalent (e.g., carbodiimidazole, triphosgene etc., preferably triphosgene). As the reagent, diphosgene, chloroethyl carbonate and the like can be used, other than the above-mentioned two kinds of reagents.

As the solvent to be used in the reaction, for example, ether solvents such as diethyl ether, tetrahydrofuran, dioxane, 1,2-dimethoxyethane, diglyme etc.; hydrocarbon solvents such as benzene, toluene, hexane, xylene etc.; halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane etc.; alcohol solvents such as methanol, ethanol, isopropyl alcohol, tert-butanol etc.; ester solvents such as ethyl acetate, methyl acetate, butyl acetate etc.; polar solvents such as acetone, N,N-dimethylformamide, dimethylsulfoxide, water etc.; and the like can be mentioned, These may be used alone or in combination. Preferable solvents for this reaction are N,N-dimethylformamide, and a mixture of THF and water.

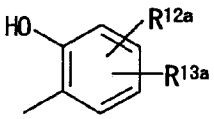
For this reaction, a base is preferably used. As the usable base, for example, inorganic bases such as sodium hydroxide, sodium hydrogen carbonate (sodium bicarbonate), potassium carbonate etc.; organic bases such as triethylamine, diazabicycloundecene, 1,8-diazabicyclo[5.4.0]undec-7-ene etc. can be mentioned, with preference given to sodium hydrogen carbonate.

The reaction temperature is generally -10°C to 60°C, preferably 0°C to room temperature.

The reaction time is generally not less than 1hr, preferably 1-24 hr, more preferably 3-24 hr, preferably 6-12 hr.

Step 2-2

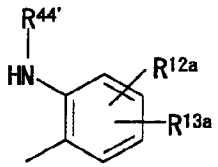
A compound represented by the formula (1-5), which is one of the object compounds, can be obtained by subjecting a compound wherein ring D is



wherein R^{12a} and R^{13a} are as defined above, from among the compounds represented by the formula (1-2) obtained in Steps 1-3 and 1-5, to the same reaction as in Step 2-1.

Step 2-3

A compound represented by the formula (1-6), which is one of the object compounds, can be obtained by reacting a compound wherein ring D is



wherein R^{12a}, R^{13a} and $R^{44'}$ are as defined above, from among the compounds represented by the formula (1-2) obtained in Steps 1-3 and 1-5, with a thiocarbonyl compound in a solvent.

As the solvent to be used in the reaction, for example, ether solvents such as diethyl ether, tetrahydrofuran, dioxane, 1,2-dimethoxyethane, diglyme etc.; hydrocarbon solvents such as benzene, toluene, hexane, xylene etc.; halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane etc.; alcohol solvents such as methanol, ethanol, isopropyl alcohol, tert-butanol etc.; ester solvents such as ethyl acetate, methyl acetate, butyl acetate etc.; polar solvents such as acetone, N,N-dimethylformamide, dimethyl sulfoxide, water etc.; and the like can be mentioned, These may be used alone or in combination. Preferable solvent for this reaction is tetrahydrofuran.

As the thiocarbonyl compound, for example, thiocarbonyldiimidazole, carbon disulfide, thiophosgene and the like can be mentioned, with preference given to thiocarbonyldiimidazole.

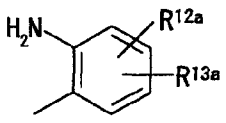
In this reaction, the use of base may be desired. As the usable base, for example, inorganic bases such as sodium hydroxide, sodium hydrogen carbonate, potassium carbonate etc.; and organic bases such as triethylamine, 1,8-diazabicyclo[5.4.0]undec-7-ene etc. can be mentioned.

The reaction temperature is generally -10°C to 60°C, preferably 0°C to room temperature.

The reaction time is generally 1-12 hr, preferably 2-6 hr.

Step 2-4

A compound represented by the formula (1-7), which is one of the object compounds, can be obtained by reacting a compound wherein ring D is



wherein R^{12a} and R^{13a} are as defined above, from among the compounds represented by the formula (1-2) obtained in Steps

1-3 and 1-5, with orthoacetic acid ester, or formic acid or a derivative thereof in a solvent, in the presence of an acid.

As the solvent, for example, ether solvents such as diethyl ether, tetrahydrofuran, dioxane, 1,2-dimethoxyethane, diglyme etc.; hydrocarbon solvents such as benzene, toluene, hexane, xylene etc.; halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane etc.; alcohol solvents such as methanol, ethanol, isopropyl alcohol, tert-butanol etc.; ester solvents such as ethyl acetate, methyl acetate, butyl acetate etc.; polar solvents such as acetone, N,N-dimethylformamide, dimethyl sulfoxide, formic acid etc.; and the like can be mentioned. These may be used alone or in combination. Preferable solvent for this reaction is N,N-dimethylformamide.

As the acid to be used in the reaction, for example, inorganic acids such as hydrochloric acid, sulfuric acid, nitric acid etc.; organic acids such as trifluoroacetic acid, trichloroacetic acid, acetic acid, methanesulfonic acid, p-toluenesulfonic acid etc. can be mentioned, with preference given to methanesulfonic acid.

As the orthoacetic acid ester, methyl orthoacetate is preferable. As the formic acid and a derivative thereof, for example, formic acid, ethyl orthoformate and the like can be mentioned, with preference given to formic acid.

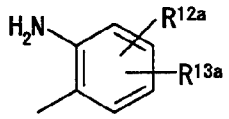
The reaction temperature is generally -10°C to 100°C, preferably 0°C to room temperature.

The reaction time is generally 30 min.-12 hr, preferably 30 min.-6 hr, more preferably 1-6 hr.

Step 2-5

A compound represented by the formula (1-8), which is one of the object compounds, can be obtained by reacting, from among the compounds represented by the formula (1-2) obtained in Step 1-3 or 1-5, a compound wherein ring D is represented

by



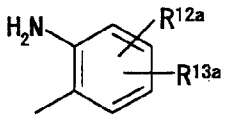
wherein R^{12a} and R^{13a} are as defined above, with formic acid under heating.

The reaction temperature is generally 80°C to 300°C, preferably 100°C to 200°C.

The reaction time is generally 4-24 hr, preferably 5-12 hr.

Step 2-6

A compound represented by the formula (1-9), can be obtained by reacting, from among the compounds represented by the formula (1-2) obtained in Step 1-3 or 1-5, a compound wherein ring D is represented by



wherein R^{12a} and R^{13a} are as defined above (i) with an acetyl halide compound (e.g., acetyl chloride, acetyl bromide etc.) in a solvent in the presence of an organic base (e.g., pyridine, triethylamine, sodium hydrogen carbonate etc.), and (ii) by cyclizing the obtained compound without isolation using a base and sodium iodide and the like.

As the solvent in (i) and (ii), for example, ether solvents such as diethyl ether, tetrahydrofuran, dioxane, 1,2-dimethoxyethane, diglyme etc.; hydrocarbon solvents such as benzene, toluene, hexane, xylene etc.; halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane etc.; alcohol solvents such as methanol, ethanol, isopropyl alcohol, tert-butanol etc.; ester solvents such as ethyl acetate, methyl acetate, butyl acetate etc.; polar solvents such as acetone, N,N-dimethylformamide,

dimethyl sulfoxide etc.; and the like can be mentioned. These may be used alone or in combination. Preferable solvents for this reaction are tetrahydrofuran, ethyl acetate, N,N-dimethylformamide, and a mixed solvent thereof.

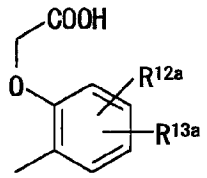
As the base to be used for the reaction, for example, alkali metal hydrides such as sodium hydride, potassium hydride etc.; alkali metal alkoxides such as sodium ethoxide, sodium methoxide, potassium tert-butoxide and the like; alkyllithiums such as n-butyllithium, sec-butyllithium etc.; alkali metal amides such as lithium diisopropylamide, sodium amide, lithium bistrimethylsilylazide etc.; alkali metal carbonates such as sodium carbonate, potassium carbonate etc.; alkali metal hydrogen carbonates such as sodium hydrogen carbonate, potassium hydrogen carbonate etc.; alkali metal hydroxides such as lithium hydroxide, sodium hydroxide, potassium hydroxide etc.; alkali metal carboxylates such as sodium acetate, potassium acetate etc.; alkali metal phosphates such as sodium phosphate, potassium phosphate etc.; and organic bases such as triethylamine, pyridine, N-methylmorpholine, 1,8-diazabicyclo[5.4.0]undec-7-ene etc. can be mentioned, with preference given to potassium carbonate.

The reaction temperature is generally -30°C to 100°C, preferably 0°C to 80°C, more preferably 0°C to room temperature.

The reaction time is generally 1-24 hr, preferably 1-15 hr, more preferably 2-12 hr.

Step 2-7

A compound represented by the formula (1-10), which is one of the object compounds, can be obtained by cyclizing, from among the compound represented by the formula (1-2) obtained in Step 1-3 or 1-5, a compound wherein ring D is



wherein R^{12a} and R^{13a} are as defined above, in a solvent in the presence of a condensing agent.

As the solvent, for example, ether solvents such as diethyl ether, tetrahydrofuran, dioxane, 1,2-dimethoxyethane, diglyme etc.; hydrocarbon solvents such as benzene, toluene, hexane, xylene etc.; halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane etc.; alcohol solvents such as methanol, ethanol, isopropyl alcohol, tert-butanol etc.; ether solvents such as ethyl acetate, methyl acetate, butyl acetate etc.; polar solvents such as acetone, N,N-dimethylformamide, dimethyl sulfoxide etc.; and the like can be mentioned. These may be used alone or in combination. Preferable solvent for this reaction is N,N-dimethylformamide.

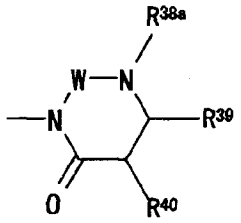
As the condensing agent, any condensing agent used for general peptide condensation method (e.g., acid chloride method, mixed acid anhydride method etc.). Of these, a combination of 1-hydroxybenzotriazole monohydrate and 1-(3-(dimethylamino)propyl)-3-ethylcarbodiimide hydrochloride is preferable.

The reaction temperature is generally -30°C to 60°C, preferably 0°C to room temperature.

The reaction time is generally 5-24 hr, preferably 10-20 hr.

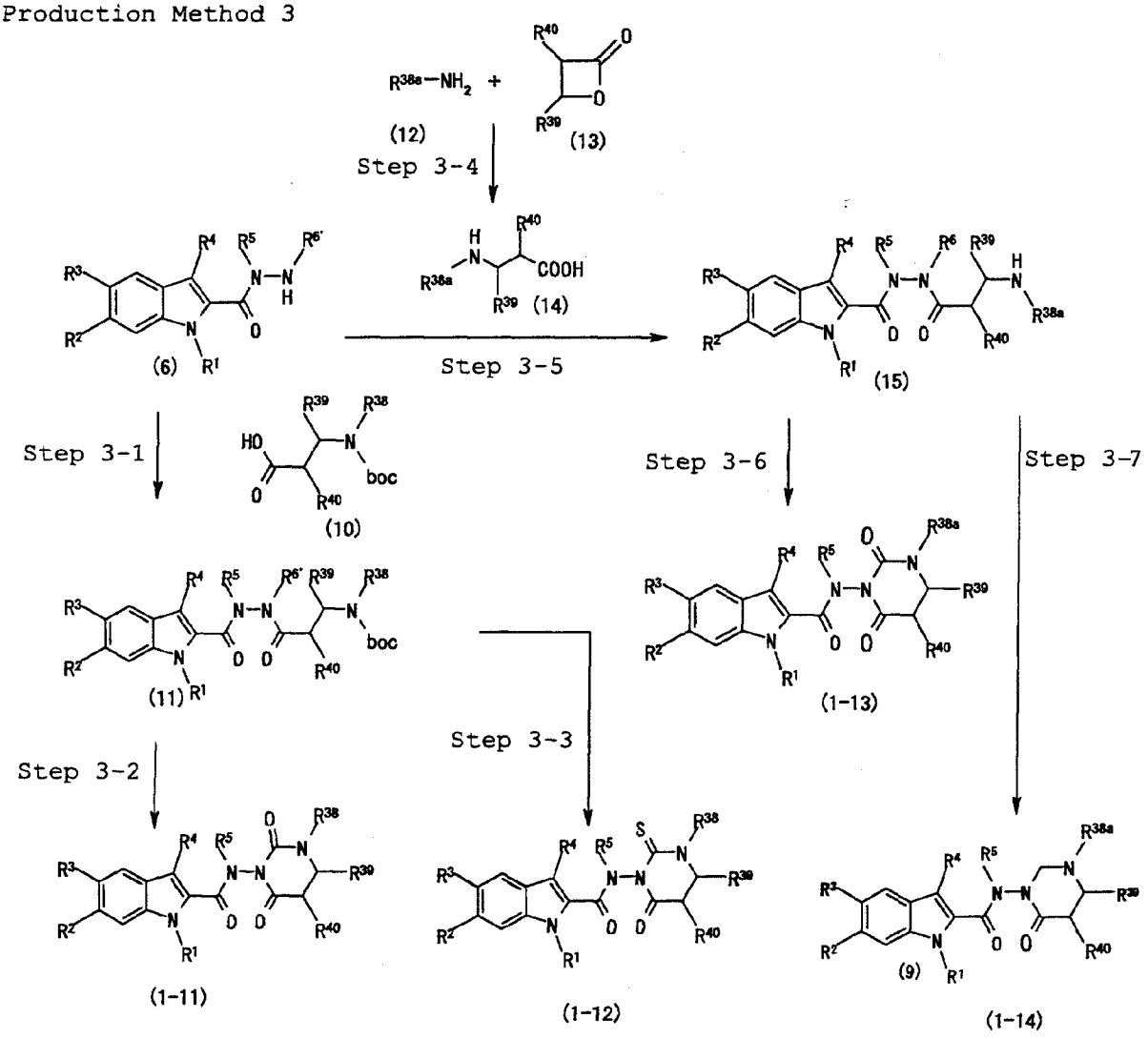
Production Method 3

A production method for a compound represented by the formula (1), wherein R^6 and R^7 form, together with the adjacent nitrogen atom,



wherein W, R^{38}, R^{39} and R^{40} are as defined above, and R^{38a} is an aryl group, is exemplarily shown in the following.

Production Method 3



wherein R^1, R^2, R^3, R^4, R^5, $R^{6'}$, R^{38}, R^{38a}, R^{39} and R^{40} are as defined above and boc is a tert-butoxycarbonyl group.

Step 3-1

A compound represented by the formula (11) can be

obtained by subjecting a compound represented by the formula (6) obtained in Step 1-2 and a compound represented by the formula (10) to a condensation reaction as in Step 1-3.

Step 3-2

A tert-butoxycarbonyl group of a compound represented by the formula (11) is deprotected with an acid (e.g., trifluoroacetic acid, hydrochloric acid, hydrobromic acid, p-toluenesulfonic acid etc.) and then the obtained amino compound is cyclized with a phosgene equivalent (e.g., carbonyldiimidazole, triphosgene etc.) in the presence of a base to give a compound represented by the formula (1-11), which is one of the object compounds.

As the solvent to be used in the reaction, for example, ether solvents such as diethyl ether, tetrahydrofuran, dioxane, 1,2-dimethoxyethane, diglyme, diphenyl ether etc.; hydrocarbon solvents such as benzene, toluene, hexane, xylene etc.; halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, chlorobenzene, 1,2-dichloroethane etc.; alcohol solvents such as methanol, ethanol, isopropyl alcohol, tert-butanol etc.; polar solvents such as N,N-dimethylformamide, dimethyl sulfoxide, water etc.; and the like can be mentioned. These may be used alone or in combination or the reaction can be carried out without solvent. Preferable solvent for this reaction is tetrahydrofuran.

As the base to be used for the reaction, for example, alkali metal hydrides such as sodium hydride, potassium hydride etc.; alkali metal alkoxides such as sodium ethoxide, sodium methoxide, potassium tert-butoxide and the like; alkyllithiums such as n-butyllithium, sec-butyllithium etc.; alkali metal amides such as lithium diisopropylamide, sodium amide, lithium bistrimethylsilylamide etc.; alkali metal carbonates such as sodium carbonate, potassium carbonate etc.; alkali metal hydrogen carbonates such as sodium hydrogen

carbonate, potassium hydrogen carbonate etc.; alkali metal hydroxides such as lithium hydroxide, sodium hydroxide, potassium hydroxide etc.; alkali metal carboxylates such as sodium acetate, potassium acetate etc.; alkali metal phosphates such as sodium phosphate, potassium phosphate etc.; and organic bases such as triethylamine, pyridine, N-methylmorpholine, 1,8-diazabicyclo[5.4.0]undec-7-ene etc. can be mentioned, with preference given to triethylamine.

The reaction temperature is generally 0°C to 100°C, preferably room temperature to 60°C.

The reaction time is generally 1-48 hr, preferably 1-25 hr, more preferably 2-24 hr.

Step 3-3

In the same manner as in Step 3-2, a tert-butoxycarbonyl group of a compound represented by the formula (11) is deprotected with an acid (e.g., trifluoroacetic acid, hydrochloric acid etc.) and then the obtained compound is cyclized in the presence of a base using a thiocarbonylating reagent (e.g., thiocarbonyldiimidazole, carbon disulfide, thiophosgene etc.) to give a compound represented by the formula (1-12), which is one of the object compounds.

Step 3-4

A compound represented by the formula (14) can be obtained by reacting a compound represented by the formula (12) with a compound represented by the formula (13) in acetonitrile.

The reaction temperature is generally 50°C to 200°C, preferably 80°C to 100°C.

The reaction time is generally 1-10 hr, preferably 2-5 hr.

Step 3-5

In the same manner as in Step 1-3, a compound represented by the formula (15) can be obtained by reacting a compound represented by the formula (6) with a compound represented by

the formula (14).

Step 3-6

A compound represented by the formula (1-13), which is one of the object compounds can be obtained by cyclizing a compound represented by the formula (15) with a phosgene equivalent (e.g., triphosgene, carbonyldiimidazole, diphosgene etc.) in a solvent in the presence of a base.

As the solvent to be used in the reaction, for example, ether solvents such as diethyl ether, tetrahydrofuran, dioxane, 1,2-dimethoxyethane, diglyme, diphenyl ether etc.; hydrocarbon solvents such as benzene, toluene, hexane, xylene etc.; halogen solvents such as dichloromethane, chloroform, chlorobenzene, carbon tetrachloride, 1,2-dichloroethane etc.; alcohol solvents such as methanol, ethanol, isopropyl alcohol, tert-butanol etc.; polar solvents such as N,N-dimethylformamide, dimethyl sulfoxide, water etc.; dimethylaniline; and the like can be mentioned. These may be used alone or in combination or the reaction can be carried out without solvent. Preferable solvent for this reaction is tetrahydrofuran.

As the base to be used for the reaction, for example, alkali metal hydrides such as sodium hydride, potassium hydride etc.; alkali metal alkoxides such as sodium ethoxide, sodium methoxide, potassium tert-butoxide and the like; alkyllithiums such as n-butyllithium, sec-butyllithium etc.; alkali metal azides such as lithium diisopropylazide, sodium amide, lithium bistrimethylsilylazide etc.; alkali metal carbonates such as sodium carbonate, potassium carbonate etc.; alkali metal hydrogen carbonates such as sodium hydrogen carbonate, potassium hydrogen carbonate etc.; alkali metal hydroxides such as lithium hydroxide, sodium hydroxide, potassium hydroxide etc.; alkali metal carboxylates such as sodium acetate, potassium acetate etc.; alkali metal

phosphates such as sodium phosphate, potassium phosphate etc.; and organic bases such as triethylamine, pyridine, N-methylmorpholine, 1,8-diazabicyclo[5.4.0]undec-7-ene etc. can be mentioned, with preference given to triethylamine.

The reaction temperature is generally 0°C to 100°C, preferably 0°C to room temperature.

The reaction time is generally 1-24 hr, preferably 4-10 hr.

Step 3-7

A compound represented by the formula (1-14), which is one of the object compounds, can be obtained by cyclizing a compound represented by the formula (15) with a formalin equivalent (e.g., paraformaldehyde, dimethoxymethane, dibromomethane etc.) in a solvent.

As the solvent to be used in the reaction, for example, ether solvents such as diethyl ether, tetrahydrofuran, dioxane, 1,2-dimethoxyethane, diglyme, diphenyl ether etc.; hydrocarbon solvents such as benzene, toluene, hexane, xylene etc.; halogen solvents such as dichloromethane, chloroform, chlorobenzene, carbon tetrachloride, 1,2-dichloroethane etc.; alcohol solvents such as methanol, ethanol, isopropyl alcohol, tert-butanol etc.; polar solvents such as N,N-dimethylformamide, dimethyl sulfoxide, water etc.; dimethylaniline and the like can be mentioned. These may be used alone or in combination or the reaction can be carried out without solvent. Preferable solvents for this reaction are methanol and ethanol.

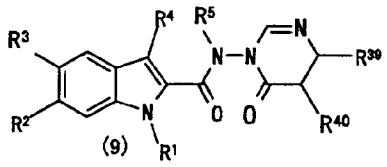
This reaction is preferably carried out in the presence of an acid or a base.

The reaction temperature is generally 0°C to 100°C, preferably 0°C to room temperature.

The reaction time is generally 1 hr-10 days, preferably 1 day-10 days, more preferably 1 day -3 days.

A compound represented by the formula (1-14) (wherein R^{38a} is a hydrogen atom) can be produced by the following method in addition to the method of the above-mentioned Step 3-7:

a compound represented by

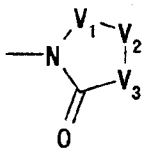


(1-14')

wherein each symbol is as defined above is reduced. The reduction can be conducted by a conventional method. For example, a compound represented by the formula (1-14') is reacted with a reducing agent such as sodium cyanoborohydride and the like to give a desired compound.

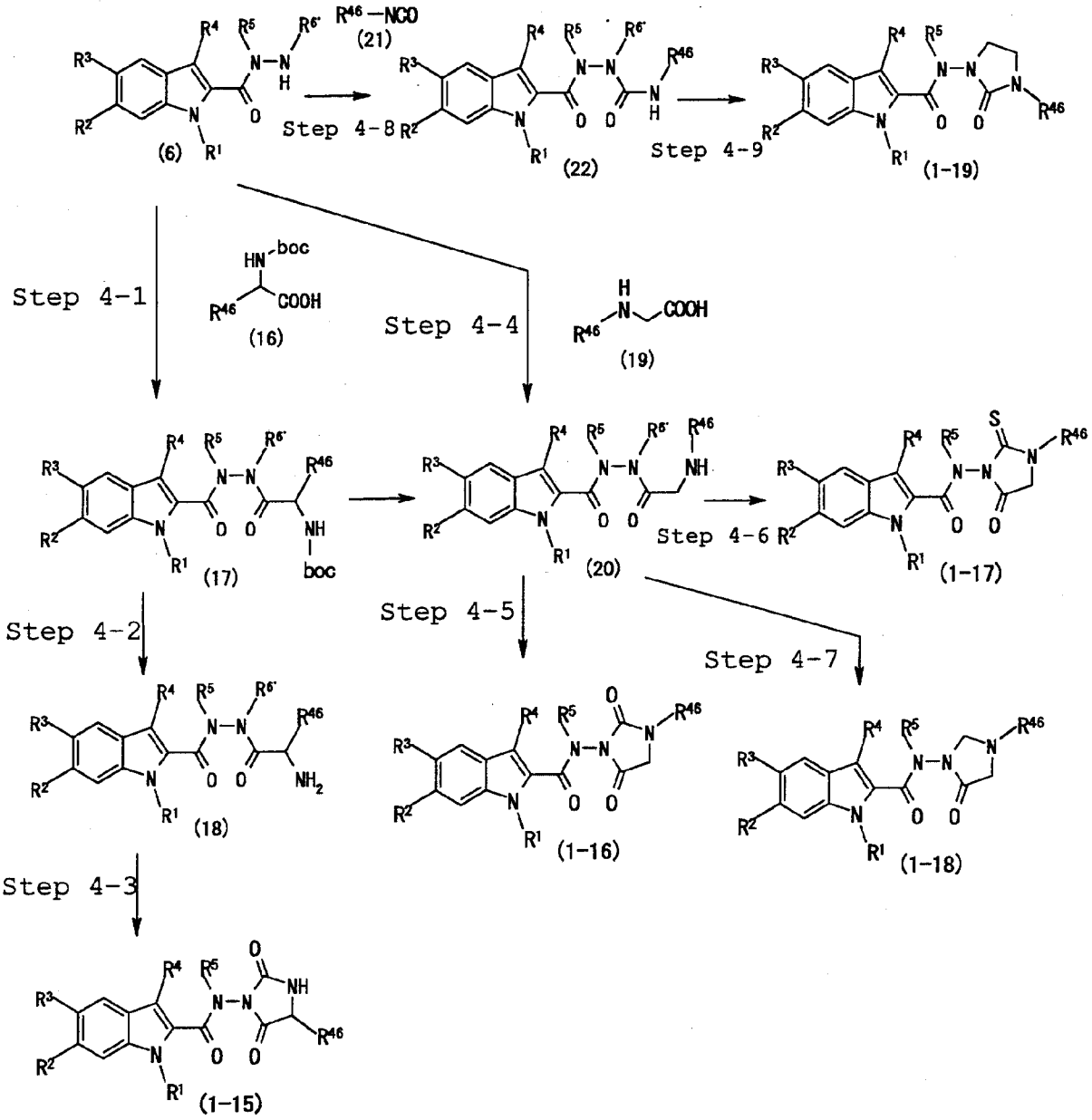
Production Method 4

A compound represented by the formula (1), wherein R^6 and R^7 form, together with the adjacent nitrogen atom,



wherein V_1, V_2 and V_3 are as defined above is exemplarily shown in the following.

Production Method 4



wherein R^1, R^2, R^3, R^4, R^5, $R^{5'}$, $R^{6'}$ and R^{46} are as defined above and boc is a tert-butoxycarbonyl group.

Step 4-1

In the same manner as in Step 1-3, a compound represented by the formula (17) can be obtained by reacting a compound represented by the formula (6) with a compound represented by the formula (16).

Step 4-2

Step 4-2

This step is deprotection of an amino-protecting group generally performed, wherein a compound represented by the formula (17) is deprotected in a solvent using an acid to give a compound represented by the formula (18).

As the solvent, for example, ether solvents such as diethyl ether, tetrahydrofuran, dioxane, 1,2-dimethoxyethane, diglyme etc.; hydrocarbon solvents such as benzene, toluene, hexane, xylene etc.; halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane etc.; alcohol solvents such as methanol, ethanol, isopropyl alcohol, tert-butanol etc.; ether solvents such as ethyl acetate, methyl acetate, butyl acetate etc.; polar solvents such as N,N-dimethylformamide, dimethyl sulfoxide etc.; and the like can be mentioned. These may be used alone or in combination or the reaction can be carried out without solvent. Preferable solvents for this reaction are dioxane, dichloroethane and trifluoroacetic acid.

As an acid to be used for the reaction, for example, inorganic acids such as hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid etc.; organic acids such as trifluoroacetic acid, trichloroacetic acid, acetic acid, methanesulfonic acid, p-toluenesulfonic acid etc. can be mentioned, with preference given to trifluoroacetic acid.

The reaction temperature is generally -10°C to 60°C, preferably 0°C to 60°C, more preferably 0°C to room temperature.

The reaction time is generally not less than 1 hr, preferably 1-20 hr, more preferably 1-12 hr, still more preferably 4-6 hr.

Step 4-3

A compound represented by the formula (1-15), which is one of the object compounds, can be obtained by cyclizing a compound represented by the formula (18) with a phosgene

equivalent (e.g., carbonyldiimidazole, triphosgene, diphosgene, ethyl chlorocarbonate etc.) in a solvent.

As the solvent, for example, ether solvents such as diethyl ether, tetrahydrofuran, dioxane, 1,2-dimethoxyethane, diglyme, diphenyl ether etc.; hydrocarbon solvents such as benzene, toluene, hexane, xylene etc.; halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane, chlorobenzene etc.; alcohol solvents such as methanol, ethanol, isopropyl alcohol, tert-butanol etc.; polar solvents such as N,N-dimethylformamide, dimethyl sulfoxide, water etc.; and the like can be mentioned. These may be used alone or in combination or the reaction can be carried out without solvent. Preferable solvent for this reaction is tetrahydrofuran.

In this reaction, the reaction may proceed smoothly when a base is used.

The reaction temperature is generally -10°C to 100°C, preferably 0°C to room temperature.

The reaction time is generally 0.5-24 hr, preferably 1-3 hr.

Step 4-4

A compound represented by the formula (20) can be obtained by cyclizing a compound represented by the formula (6) with a compound represented by the formula (19) in the same manner as in Step 1-3.

Step 4-5

In the same manner as in Step 4-3, a compound represented by the formula (20) is cyclized with a phosgene equivalent (e.g., carbonyldiimidazole, triphosgene, diphosgene, ethyl chlorocarbonate etc.) to give a compound represented by the formula (1-16), which is one of the object compounds.

Step 4-6

A compound represented by the formula (1-17), which is

one of the object compounds, can be obtained by cyclizing a compound represented by the formula (20) with a thiocarbonylating reagent (e.g., thiocarbonyldiimidazole, carbon disulfide, thiophosgene etc.) in the same manner as in Step 3-3.

Step 4-7

A compound represented by the formula (1-18), which is one of the object compounds, can be obtained by cyclizing a compound represented by the formula (20) with a formalin equivalent (e.g., paraformaldehyde, dimethoxymethane, dibromomethane etc.) in the same manner as in Step 3-7.

Step 4-8

In the same manner as in Step 1-3, a compound represented by the formula (22) can be obtained by reacting a compound represented by the formula (6) with a compound represented by the formula (21).

Step 4-9

A compound represented by the formula (1-19), which is one of the object compounds, can be obtained by reacting a compound represented by the formula (22) with 1,2-dibromoethane or 1,2-dichloroethane in a solvent in the presence of a base.

One of 1,2-dibromoethane and 1,2-dichloroethane is used for the reaction.

As the solvent, for example, ether solvents such as diethyl ether, tetrahydrofuran, dioxane, 1,2-dimethoxyethane, diglyme, diphenyl ether etc.; hydrocarbon solvents such as benzene, toluene, hexane, xylene etc.; halogen solvents such as chlorobenzene etc.; alcohol solvents such as methanol, ethanol, isopropyl alcohol, tert-butanol etc.; polar solvents such as N,N-dimethylformamide, dimethyl sulfoxide etc.; and the like can be mentioned. These may be used alone or in combination or the reaction can be carried out without solvent.

Preferable solvent for this reaction is N,N-dimethylformamide.

As the base to be used for the reaction, for example, alkali metal hydrides such as sodium hydride, potassium hydride etc.; alkali metal alkoxides such as sodium ethoxide, sodium methoxide, potassium tert-butoxide and the like; alkyllithiums such as n-butyllithium, sec-butyllithium etc.; alkali metal amides such as lithium diisopropylamide, sodium amide, lithium bistrimethylsilylazide etc.; alkali metal carbonates such as sodium carbonate, potassium carbonate etc.; alkali metal hydrogen carbonates such as sodium hydrogen carbonate, potassium hydrogen carbonate etc.; alkali metal hydroxides such as lithium hydroxide, sodium hydroxide, potassium hydroxide etc.; alkali metal carboxylates such as sodium acetate, potassium acetate etc.; alkali metal phosphates such as sodium phosphate, potassium phosphate etc.; and organic bases such as triethylamine, pyridine, N-methylmorpholine, 1,8-diazabicyclo[5.4.0]undec-7-ene etc. can be mentioned, with preference given to potassium carbonate.

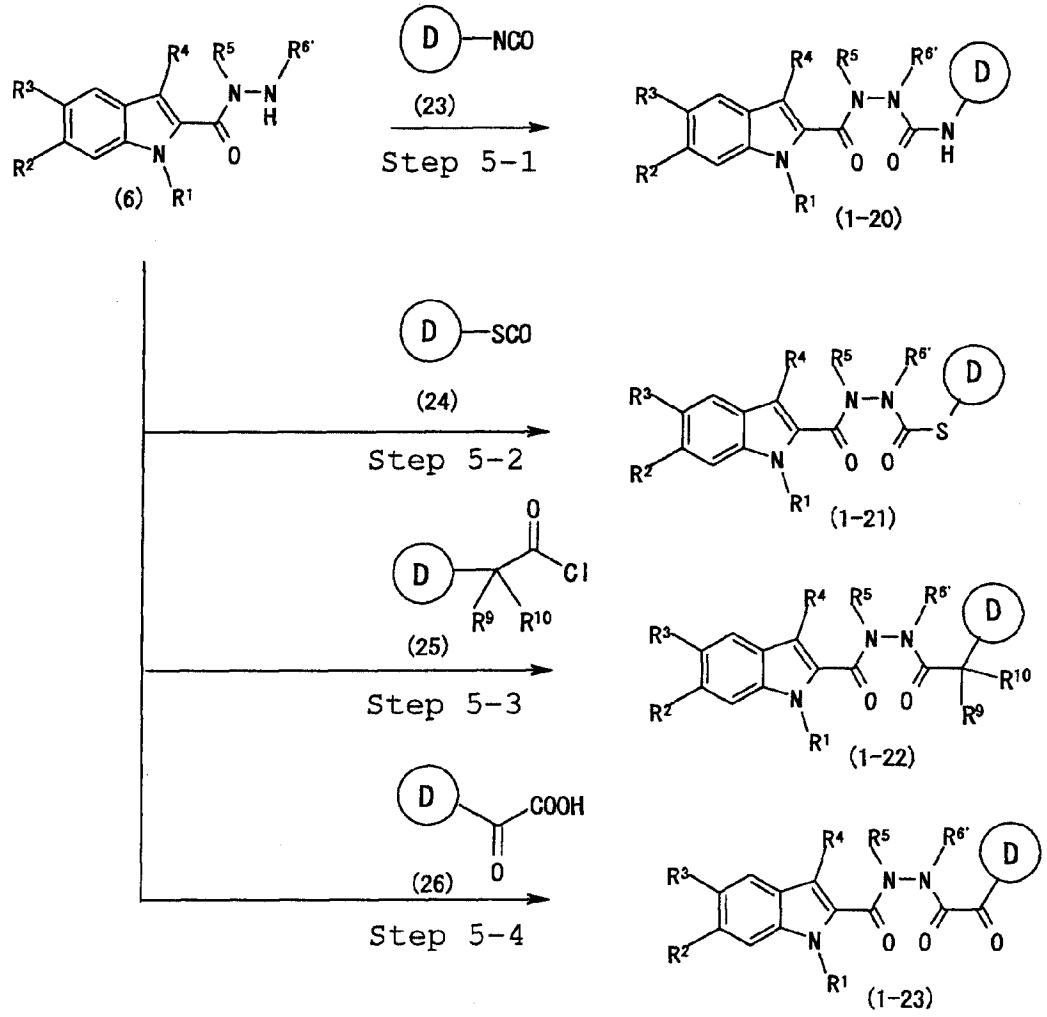
The reaction temperature is generally 0°C to 100°C, preferably room temperature to 70°C.

The reaction time is generally 1-48 hr, preferably 2-24 hr.

Production Method 5

A production method of a compound represented by the formula (1) wherein R^7 is $-C(=O)-A'-$ wherein A' is $-N(R^8)-$, $-C(R^9)(R^{10})-$ or $-CO-$ and ring D is as defined above is exemplarily shown in the following.

Production Method 5



wherein R^1, R^2, R^3, R^4, R^5, $R^{6'}$, R^9, R^{10} and ring D are as defined above.

Step 5-1

A compound represented by the formula (1-20), which is one of the object compounds, can be obtained by reacting a compound represented by the formula (6) obtained in Step 1-2 with a compound represented by the formula (23) in a solvent.

As the solvent, for example, ether solvents such as diethyl ether, tetrahydrofuran, dioxane, 1,2-dimethoxyethane, diglyme, diphenyl ether etc.; hydrocarbon solvents such as benzene, toluene, hexane, xylene etc.; halogen solvents such as dichloromethane, chloroform, carbon tetrachloride,

chlorobenzene, 1,2-dichloroethane, etc.; alcohol solvents such as methanol, ethanol, isopropyl alcohol, tert-butanol etc.; polar solvents such as N,N-dimethylformamide, dimethyl sulfoxide, etc.; dimethylaniline; and the like can be mentioned. These may be used alone or in combination or the reaction can be carried out without solvent. Preferable solvent for this reaction is dioxane.

The reaction temperature is generally 0°C to 100°C, preferably room temperature to 80°C.

The reaction time is generally 1-12 hr, preferably 1-6 hr, more preferably 2-6 hr.

Step 5-2

A compound represented by the formula (1-21), which is one of the object compounds, can be obtained by reacting a compound represented by the formula (6) with a compound represented by the formula (24) in the same manner as in Step 5-1.

Step 5-3

A compound represented by the formula (1-22), which is one of the object compounds, can be obtained by reacting a compound represented by the formula (6) with a compound represented by the formula (25) in a solvent in the presence of a base.

As the solvent, for example, ether solvents such as diethyl ether, tetrahydrofuran, dioxane, 1,2-dimethoxyethane, diglyme, diphenyl ether etc.; hydrocarbon solvents such as benzene, toluene, hexane, xylene etc.; halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, chlorobenzene, 1,2-dichloroethane, etc.; alcohol solvents such as methanol, ethanol, isopropyl alcohol, tert-butanol etc.; polar solvents such as N,N-dimethylformamide, dimethyl sulfoxide, etc.; and the like can be mentioned. These may be used alone or in combination or the reaction can be carried

out without solvent. Preferable solvent for this reaction is tetrahydrofuran.

As the base to be used for the reaction, for example, alkali metal hydrides such as sodium hydride, potassium hydride etc.; alkali metal alkoxides such as sodium ethoxide, sodium methoxide, potassium tert-butoxide and the like; alkyllithiums such as n-butyllithium, sec-butyllithium etc.; alkali metal carbonates such as sodium carbonate, potassium carbonate etc.; alkali metal hydrogen carbonates such as sodium hydrogen carbonate, potassium hydrogen carbonate etc.; alkali metal hydroxides such as lithium hydroxide, sodium hydroxide, potassium hydroxide etc.; alkali metal carboxylates such as sodium acetate, potassium acetate etc.; alkali metal phosphates such as sodium phosphate, potassium phosphate etc.; and organic bases such as triethylamine, pyridine, N-methylmorpholine etc. can be mentioned, with preference given to triethylamine.

The reaction temperature is generally 0°C to 100°C, preferably room temperature to 60°C.

The reaction time is generally 1-12 hr, preferably 1-6 hr, more preferably 2-6 hr.

Step 5-4

In the same manner as in Step 1-3, a compound represented by the formula (1-23), which is one of the object compounds, can be obtained by reacting a compound represented by the formula (6) with a compound represented by the formula (26).

When a salt of the compound (1) of the present invention is desired, a free compound (1) of the present invention obtained in the above-mentioned Production Method 1-5 can be converted to a salt according to conventional methods.

Examples

The present invention is explained in detail by referring to Examples, which are not to be construed as

limitative. In the following formulas, "boc" means tert-butoxycarbonyl.

Example 1

benzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide

a) 5-chloro-1H-indole-2-carboxylic acid hydrazide

5-Chloro-1H-indole-2-carboxylic acid (1.96 g) and 1-hydroxybenzotriazole monohydrate (HOBt·H_2O) (1.58 g) were dissolved in N,N-dimethylformamide (DMF) (10 ml) and 1-(3-(dimethylamino)propyl)-3-ethylcarbodiimide hydrochloride (EDC) (2.58 g) was added. This solution was stirred at room temperature for 3 hr. This solution was cooled in an ice-bath and hydrazine hydrate (2.4 ml) was added. This solution was stirred at room temperature for 11 hr. Water (20ml) was added slowly to this reaction mixture. The precipitated solid was collected by filtration and dried in vacuo to give the title compound (2.24 g) (containing DMF (15%) as a residual solvent). This sample was boiled in tetrahydrofuran (THF), allowed to cool and filtered to give a purer sample.

^{1}H-NMR(δ, 300MHz, DMSO-d_6).

4.52(2H,brs), 7.05(1H,d,J=1.5Hz), 7.16(1H,dd,J=8.7Hz,2.1Hz), 7.42(1H,d,J=8.7Hz), 7.66(1H,d,J=1.9Hz), 9.86(1H,brs), 11.84(1H,s).

b) benzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide

5-Chloro-1H-indole-2-carboxylic acid hydrazide (98 mg) obtained in Example 1 a) was suspended in THF (2 ml) and triethylamine (73 μl) was added. This mixture was cooled in an ice-bath and benzoyl chloride (61 μl) was added slowly. The reaction mixture was stirred at room temperature for 10 min. Thereto were added ethyl acetate (5 ml), THF (3 ml) and ice water (10 ml) and the mixture was stirred. The separated organic layer was washed successively with aqueous sodium hydroxide solution (0.1N) and water and dried over anhydrous sodium sulfate. This solution was filtered and concentrated to allow precipitation of white crystals, which were collected by

filtration and dried in vacuo to give the title compound (29 mg) (see Table 1).

Example 1-2

2-amino-benzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide

5-Chloro-1H-indole-2-carboxylic acid hydrazide obtained in Example 1 a) (6.00 g), anthranilic acid (3.42 g) and HOBt·H_2O (3.882 g) were suspended in DMF (100 ml) and EDC (4.79 g) was added. This mixture was stirred at room temperature for one day. To the reaction mixture were added THF (200 ml) and half-saturated brine (200 ml). The separated organic layer was washed successively with aqueous sodium hydroxide solution (0.1N), aqueous hydrochloric acid (0.5N) and pure water. This solution was dried over anhydrous sodium sulfate and filtrated. This solution was concentrated to a small amount and left standing to allow precipitation of a white powder, which was collected by filtration and dried in vacuo to give the title compound (4.35 g, yield 55%) (see Table 1).

Example 1-3

2-hydroxy-benzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide

The title compound was obtained as crystals according to the same method as Example 1-2 but using salicylic acid instead of anthranilic acid (see Table 1).

Example 1-4

3-[{2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenyl}carbamoyloxy]-2,2-dimethylpropionic acid

a) 3-hydroxy-2,2-dimethylpropionic acid benzyl ester

Hydroxypivalic acid (5.03 g) was dissolved in DMF (50 ml) and benzyl bromide (5.50 ml) and potassium carbonate (11.38 g) were successively added. The mixture was stirred at room temperature for 12 hr. Water (100 ml) was added to the

reaction mixture and the mixture was extracted with ether (2×100 ml). The organic layer was washed successively with water (2×50 ml) and saturated aqueous sodium chloride solution (50 ml), dried and concentrated under reduced pressure. The obtained oily substance was purified by column chromatography to give the title compound (6.54 g) as a colorless oil.

^{1}H-NMR(δ, 300MHz, $CDCl_3$)

1.22(6H,s),2.37(1H,t,J=6.8Hz),3.58(2H,d,J=6.8Hz),5.15(2H,s),7.30-7.40(5H,m).

b) 2-(2-benzyloxycarbonyl-2-methylpropoxycarbonylamino)benzoic acid

tert-Butyl phthalate (5.38 g) was dissolved in toluene (50 ml). To this solution were successively added triethylamine (3.7 ml) and diphenylphosphoryl azide (5.7 ml) and the mixture was heated to 130°C and stirred for 1 hr. The reaction mixture was allowed to cool to room temperature and 3-hydroxy-2,2-dimethylpropionic acid benzyl ester obtained in Example 1-4 a) (4.95 g) was added. The mixture was stirred at room temperature for 17 hr. The reaction mixture was diluted with ethyl acetate (50 ml), washed successively with water (50 ml) and saturated aqueous sodium chloride solution (5 ml), dried and concentrated under reduced pressure. The obtained oily substance was purified by silica gel column chromatography (n-hexane/ethyl acetate=1:1). The oily substance (3.28 g) after purification was dissolved in dichloromethane (30 ml). This solution was cooled to 0°C and trifluoroacetic acid (30 ml) was added. The mixture was heated to room temperature and stirred for 3 hr. The reaction mixture was concentrated under reduced pressure, after which water (50 ml) was added, and the mixture was extracted with ethyl acetate (150 ml). The organic layer was washed successively with water (50 ml×3) and saturated aqueous sodium chloride solution (50 ml), dried and concentrated under reduced

pressure. The obtained oily substance was purified by column chromatography to give the title compound (2.54 g, yield 89%) as a colorless oil.

^{1}H-NMR(δ, 300MHz, DMSO-d_6)

1.22(6H,s),4.20(2H,s),5.13(2H,s),7.12(1H,m),7.25-7.34(5H,m),7.60(1H,m),
7.99(1H,dd,J=1.6,7.9Hz),8.23(1H,d,J=7.9Hz),10.72(1H,s),13.63(1H,brs).

c) 3-[{2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenyl}carbamoyloxy]-2,2-dimethylpropionic acid benzyl ester

5-Chloro-1H-indole-2-carboxylic acid hydrazide (containing 14% DMF) obtained in Example 1 a) (1.59 g), 2-(2-benzyloxycarbonyl-2-methylpropoxycarbonylamino)benzoic acid obtained in Example 1-4 b) (2.54 g) and HOBt·H_2O (1.23 g) were dissolved in DMF (25 ml). To this solution was added EDC (1.59 g), and the mixture was stirred at room temperature for 3 hr. The reaction mixture was diluted with ethyl acetate (150 ml) and washed with water (50 ml) and saturated aqueous sodium chloride solution (50 ml). This solution was dried over anhydrous sodium sulfate and concentrated under reduced pressure. The obtained solid was washed with ether in a slurry form to give the title compound (2.58 g, yield 78%) as a colorless amorphous form.

^{1}H-NMR(σ, 300MHz, DMSO-d_6)

1.20(6H,s),4.18(2H,s),5.11(2H,s),7.14-7.29(8H,m),7.48(1H,d,J=8.8Hz),
7.60(1H,d,J=7.3Hz),7.77(1H,d,J=1.8Hz),7.91(1H,d,J=7.3Hz),8.24(1H,d,J=8.4Hz),10.62(1H,s),10.72(1H,s),10.82(1H,s),11.97(1H,s).

d) 3-[{2-(2-(5-chloro-1H-indole-2-carbonyl)hydrazinocarbonyl)phenyl}carbamoyloxy]-2,2-dimethylpropionic acid

3-[{2-(2-(5-Chloro-1H-indole-2-

carbonyl)hydrazinocarbonyl)phenyl}carbamoyloxy]-2,2-dimethylpropionic acid benzyl ester obtained in Example 1-4 c) (1.64 g) was dissolved in THF (50 ml). To this solution was added 10% palladium-carbon (224 mg) and the mixture was stirred under a hydrogen atmosphere at room temperature for 6 hr and 30 min. The reaction mixture was filtered through a glass filter packed with celite and the residue was washed with THF (25 ml). The filtrate and washings were combined and concentrated under reduced pressure. The obtained solid was crystallized from ethanol to give the title compound (831 mg, yield 60%) as colorless needle crystals (see Table 1).

Example 1-5

benzoic acid 2-(5-chloro-1H-indole-2-carbonyl)-1-methylhydrazide

a)benzoic acid 1-methylhydrazide

To a solution (10 ml) of benzoic acid (500 mg) in DMF were added 1-hydroxybenzotriazole (752 mg) and EDC (942 mg), and the mixture was stirred at room temperature for 3 hr. Then, methylhydrazine (2.18 ml) was added to the reaction solution under ice-cooling. The mixture was stirred at room temperature for 16 hr, and water was added. This mixture was extracted with ethyl acetate and the organic layer was washed successively with saturated aqueous sodium hydrogen carbonate, water and saturated brine and dried over sodium sulfate. This solution was filtered, concentrated under reduced pressure and the residue was purified by silica gel column chromatography (n-hexane :ethyl acetate=1:2) to give the title compound (213 mg, yield 35%).

^{1}H-NMR (δ, 300MHz,DMSO-d_6).

3.16(3H,s),4.77(1H,brs),5.10(1H,brs),7.32-7.52(5H,m).

b) benzoic acid 2-(5-chloro-1H-indole-2-carbonyl)-1-methylhydrazide

To a solution (10 ml) of 5-chloro-1H-indole-2-carboxylic

acid (100 mg) and benzoic acid 1-methylhydrazide obtained in Example 1-5 a) (130 mg) in DMF were added 1-hydroxybenzotriazole (122 mg) and EDC (153 mg). The mixture was stirred at room temperature for 16 hr and water was added to the reaction solution. The precipitated solid was collected by filtration and washed with water and diethyl ether. The resulting solid was dried in vacuo to give the title compound (144 mg, yield 66%) (see Table 1).

Example 1-6

benzoic acid 2-(1-acetyl-5-chloro-1H-indole-2-carbonyl)hydrazide

a) 1-acetyl-5-chloro-1H-indole-2-carboxylic acid

5-Chloro-1H-indole-2-carboxylic acid (5.50 g) was dissolved in dry DMF (50 ml) and ice-cooled. Sodium hydride (60% in oil) (2.35 g) was added to this solution. The mixture was stirred at room temperature for 20 min. This solution was cooled again in an ice bath and acetyl chloride (2.3 ml) was added dropwise. This solution was stirred at room temperature for 1 hr, and cooled in an ice bath. Acetic acid (4 ml) was added to this solution, after which ethyl acetate and ice water (each 200 ml) were added. The separated organic layer was washed with water and dried over anhydrous sodium sulfate. The extract solution was filtered and concentrated. The thick solution was stood to give pale-yellow crystals. The crystals were collected by filtration and dried in vacuo to give the title compound (3.12 g, yield 49%).

^{1}H-NMR (δ, 300MHz, DMSO-d_6).

2.77(3H,s), 7.37(3H,s), 7.49(1H,m), 7.82(1H,m), 7.97(1H,d)

b) benzoic acid 2-(1-acetyl-5-chloro-1H-indole-2-carbonyl)hydrazide

In the same manner as in Example 1-5, the title compound (yield 17%) was obtained by reacting 1-acetyl-5-chloro-1H-indole-2-carboxylic acid with benzoic acid hydrazide (see

Table 1).

Example 1-7

5-chloro-1H-indole-2-carboxylic acid 2-(imino-phenyl-methyl)hydrazide

a) thiobenzimide acid methyl ester hydroiodic acid salt

To a solution (60 ml) of thiobenzamide (10.0 g) in acetone was added methyl iodide (10.3 g) at room temperature. This solution was stirred at room temperature for 13 hr. The precipitated crystals were collected by filtration, washed with diethyl ether and dried in vacuo to give the title compound (18.5 g, yield 91%).

b) 5-chloro-1H-indole-2-carboxylic acid 2-(imino-phenyl-methyl)hydrazide

To a suspension (700 ml) of 5-chloro-1H-indole-2-carboxylic acid hydrazide obtained in Example 1 a) (70.0 g) in methanol (MeOH) was added thiobenzimide acid methyl ester hydroiodic acid salt obtained in Example 1-7 a) (84.2 g) at room temperature. This suspension was stirred at room temperature for 19 hr. To the reaction mixture was added aqueous sodium hydrogen carbonate to alkalize the mixture. The precipitated solid was collected by filtration, washed with water and washed with diethyl ether. The product collected by filtration was boiled in THF-MeOH and allowed to cool. Diisopropyl ether was added and the precipitated solid was collected by filtration and dried to give the title compound (76.8 g, yield 85%) (see Table 1).

Example 1-8

5-aminothiazole-4-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide

a) 5-aminothiazole-4-carboxylic acid hydrazine

5-Amino-thiazole-4-carboxylic acid ethyl ester (460 mg) obtained in the same manner as in Chem. Pharm. Bull, 19(1) 119-123 (1971) was dissolved in ethanol (7 ml). Hydrazine

monohydrate (1.3 ml) was added to this solution and the mixture was refluxed at 100°C for 22 hr. The reaction mixture was cooled to room temperature and the obtained solid was collected by filtration and washed with ethanol. This solid was dried in vacuo to give the title compound (280 mg).

^{1}H-NMR(σ, 300MHz, DMSO-d6)

4.26(2H,s),7.07(2H,s),8.00(1H,s),8.83(1H,s).

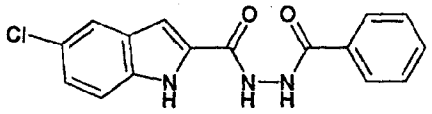
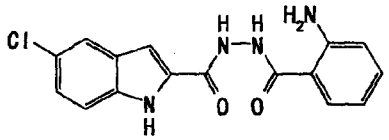
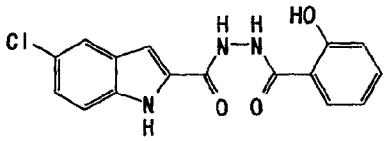
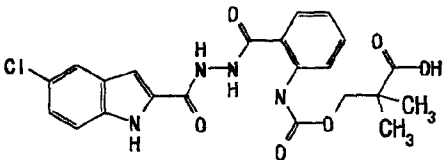
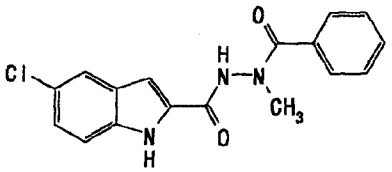
b) 5-aminothiazole-4-carboxylic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide

In the same manner as in Example 1-2, 5-chloro-1H-indole-2-carboxylic acid was reacted with 5-aminothiazole-4-carboxylic acid hydrazine obtained in Example 1-7 a) to give the title compound (yield 79%) (see Table 1).

Examples 1-9 to 1-143

In the same manner as in Examples 1 to 1-8, the compounds of Examples 1-9 to 1-143 were obtained. The obtained compounds are shown in Tables 1-18.

Table-1

Ex.	Structural formula	^{1}H-NMR(δ,300MHz,DMSO-d6)
1		7.21-7.26(2H,m), 7.48-7.64(4H,m), 7.76(1H,dJ=1.8Hz), 7.95 (2H,d,J=7.2Hz), 10.57(2H,br s), 11.83(1H,s).
1-2		6.45(2H,brs), 6.56(1H,dd,J=7.7,7.7Hz), 6.75(1H,d,J=7.7Hz,1.0H), 7.18-7.25(3H,m), 7.46(1H,d,J=8.4Hz), 7.63(1H,d,J=7.7Hz), 7.75(1H,d,J=1.8Hz), 10.19(1H,brs), 10.47(1H,s,), 11.92(1H,s).
1-3		6.98(1H,m), 6.99(1H,d,J=8.4Hz,1.0Hz), 7.23(1H,dd,J=8.4Hz,1.9Hz), 7.27(1H,d,J=1.9Hz), 7.47(1H,d,J=8.4Hz), 7.49(1H,m), 7.77(1H,d,J=1.9Hz), 7.94(1H,dd,J=7.8Hz,1.5Hz), 10.70(1H,brs), 10.77(1H,s,), 11.92(1H,brs), 11.97(1H,s).
1-4		—
1-5		3.25(3H,s), 6.98(1H,s), 7.19(1H,d,J=8.7Hz), 7.34-7.39(4H,m), 7.53-7.55(2H,m), 7.71(1H,s), 11.16(1H,s), 11.89(1H,s).

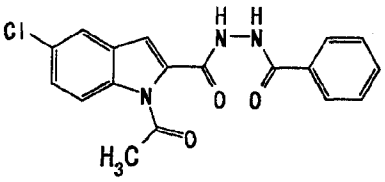
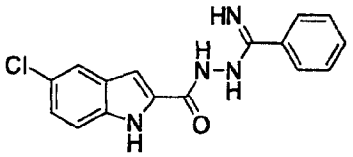
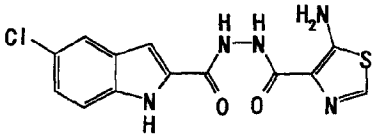
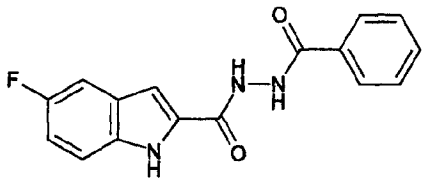
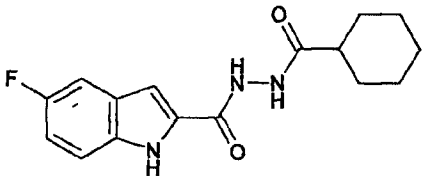
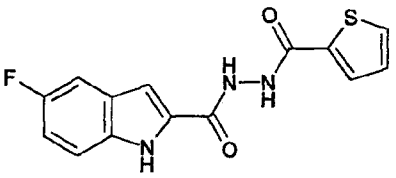
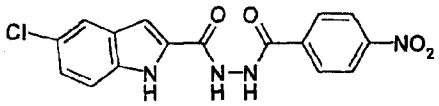
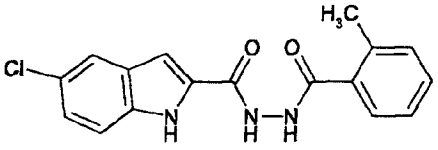
1-6		2.54(3H,s), 7.21-7.27(2H,m), 7.45-7.73(5H,m), 7.92(2H,d,J=7.5Hz), 11.40(1H,s), 12.14(1H,s).
1-7		6.82(2H,brs), 7.17-7.26(2H,m), 7.43-7.47(4H,m), 7.72(1H,s), 7.86(2H,m), 10.09(1H,brs), 11.83(1H,brs).
1-8		7.19-7.24(4H,m), 7.74(1H,m), 8.09(1H,m), 9.75(1H,s), 10.40(1H,s), 11.90(1H,s).

Table-2

Ex.	Structural formula	^{1}H-NMR(δ,300MHz,DMSO-d6)
1-9		7.09(1H,m), 7.27(1H,s), 7.44-7.64(5H,m), 7.93-7.96(2H,m), 10.54(1H,s), 10.58(1H,s), 11.84(1H,s).
1-10		1.16-1.47(5H,m), 1.64-1.76(5H,m), 2.27(1H,m), 7.06(1H,m), 7.18(1H,s), 7.40-7.46(2H,m), 9.79(1H,s), 10.34(1H,s), 11.75(1H,s).
1-11		7.09(1H,m), 7.22-7.25(2H,m), 7.44-7.48(2H,m), 7.87-7.92(2H,m), 10.57(1H,s), 10.58(1H,s), 11.85(1H,s).
1-12		7.23(1H,dd,J=2.0,8.7Hz), 7.28(1H,s), 7.47(1H,d,J=8.7Hz), 7.77(1H,d,J=2.0Hz), 8.18(2H,d,J=8.8Hz), 8.40(2H,d,J=8.8Hz), 10.76(1H,s), 10.92(1H,s), 11.97(1H,s).
1-13		2.45(3H,s), 7.21-7.32(4H,m), 7.38-7.48(3H,m), 7.76(1H,d,J=1.9Hz), 10.22(1H,s), 10.63(1H,s), 11.96(1H,s).

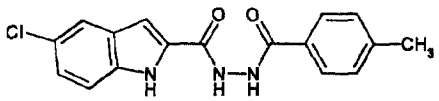
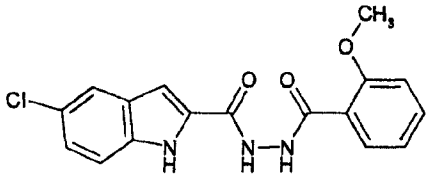
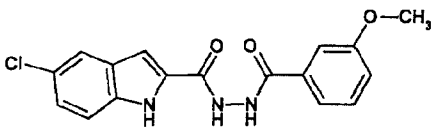
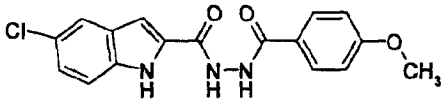
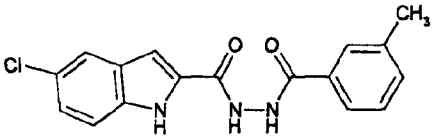
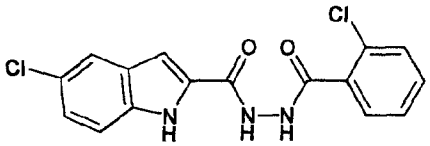
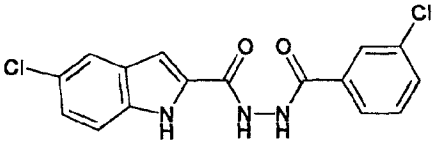
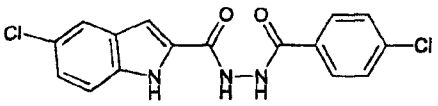
1-14		2.39(3H,s), 7.22(1H,dd,J=8.7Hz,2.0Hz), 7.26(1H,s), 7.34(2H,d,J=8.1Hz), 7.47(1H,d,J=8.7Hz), 7.76(1H,d,J=2.0Hz,1.0H), 7.85(2H,d,J=8.1Hz), 10.47(1H,s), 10.58(1H,s,11.94(1H,s).
1-15		3.92(3H,s), 7.09(1H,dd,J=7.5Hz,7.5Hz), 7.18-7.24(2H,m), 7.27(1H,s), 7.47(1H,d,J=8.8Hz), 7.53(1H,m), 7.76(1H,s), 7.77(1H,m), 10.07(1H,s), 10.72(1H,s), 11.92(1H,s).
1-16		3.83(3H,s), 7.17-7.24(2H,m), 7.26(1H,s), 7.42-7.54(4H,m), 7.76(1H,d,J=1.7Hz), 10.54(1H,brs), 10.62(1H,brs), 11.94(1H,s).

Table-3

Ex.	Structural formula	^{1}H-NMR(δ,300MHz,DMSO-d6)
1-17		3.84(3H,s), 7.07(2H,d,J=8.8Hz), 7.22(1H,dd,J=1.9,8.8Hz), 7.25(1H,s),7.47(1H,d,J=8.8Hz),7.76(1H,d,J=1.9Hz), 7.93(2H,d,J=8.8Hz), 10.40(1H,brs), 10.55(1H,brs), 11.93(1H,s).
1-18		2.39(3H,s), 7.23(1H,dd,J=2.0,8.7Hz), 7.26(1H,s), 7.41-7.48(3H,m), 7.74-7.77(2H,m), 7.77(1H,s), 10.50(1H,brs), 10.60(1H,brs), 11.94(1H,s).
1-19		7.23(1H,dd,J=8.8Hz,2.0Hz), 7.27(1H,s), 7.45-7.59(5H,m), 7.76(1H,d,J=2.0Hz), 10.45(1H,s), 10.74(1H,s), 11.95(1H,s).
1-20		6.99(1H,s), 7.15(1H,dd,J=8.7Hz,2.0Hz), 7.41-7.51(3H,m), 7.67(1H,d,J=2.0Hz), 7.87(1H,d,J=7.3Hz), 7.93(1H,s), 10.65(2H,brs), 11.80(1H,brs).
1-21		7.21(1H,dd,J=2.0,8.7Hz), 7.23(1H,s), 7.47(1H,d,J=8.7Hz), 7.61(2H,d,J=8.5Hz), 7.75(1H,d,J=2.0Hz), 7.96(2H,d,J=8.5Hz), 10.68(2H,brs), 11.97(1H,brs).

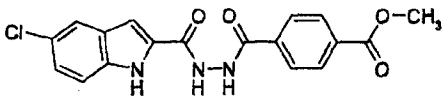
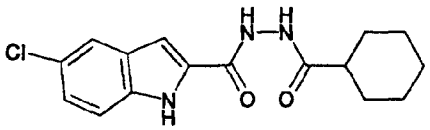
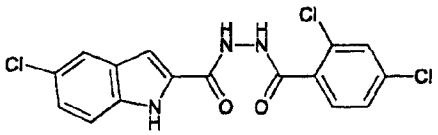
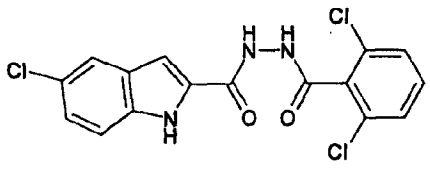
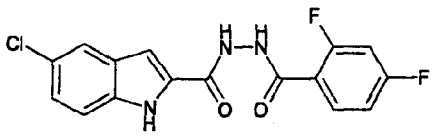
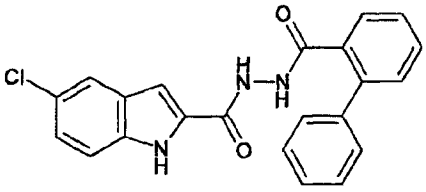
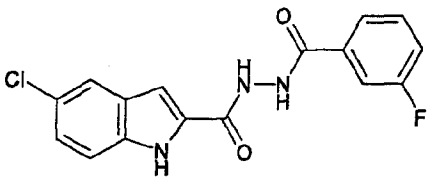
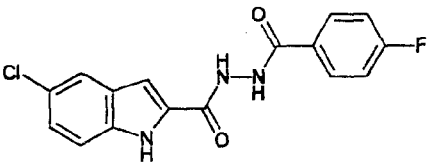
1-22		3.91(3H,s), 7.23(1H,dd,J=2.0,8.8Hz), 7.27(1H,s), 7.47(1H,d,J=8.8Hz), 7.76(1H,d,J=2.0Hz), 8.06(2H,d,J=8.6Hz), 8.11(2H,d,J=8.6Hz), 10.70(2H,brs), 11.94(1H,s).
1-23		1.15-1.75(10H,m), 2.25(1H,m), 7.09(1H,s), 7.17(1H,dd,J=8.7,2.0Hz), 7.43(1H,d,J=8.7Hz), 7.68(1H,d,J=2.0Hz), 10.28(1H,brs), 10.57(1H,brs), 11.63(1H,brs).
1-24		7.23(1H,dd,J=1.8,8.8Hz), 7.27(1H,s), 7.47(1H,d,J=8.8Hz), 7.59(1H,s), 7.59(1H,s), 7.76- 7.77(2H,m), 10.52(1H,brs), 10.75(1H,brs), 11.94(1h,s).

Table-4

Ex.	Structural formula	^{1}H-NMR(δ,300MHz,DMSO-d6)
1-25		7.22(1H,dd,J=1.9,8.6Hz), 7.31(1H,s), 7.44-7.58(4H,m), 7.76(1H,d,J=1.9Hz), 10.75(1H,s), 10.80(1H,s), 11.96(1H,s).
1-26		7.21-7.29(3H,m), 7.40-7.48(2H,m), 7.73-7.81(2H,m), 10.41(1H,brs), 10.70(1H,brs), 11.93(1H,s).
1-27		7.23(1H,dd,J=2.0,8.7Hz), 7.25(1H,s), 7.33-7.39(2H,m), 7.47(1H,d,J=8.7Hz), 7.60-7.72(2H,m), 7.76(1H,d,J=2.0Hz), 10.40(1H,brs), 10.69(1H,brs), 11.94(1H,s).
1-28		7.23(1H,dd,J=2.0,8.8Hz), 7.26(1H,s), 7.47(1H,d,J=8.8Hz), 7.48(1H,m), 7.61(1H,m), 7.77(1H,d,J=2.0Hz), 7.82-7.71(2H,m), 10.67(1H,s), 10.68(1H,s), 11.96(1H,s).
1-29		7.23(1H,dd,J=2.0,8.8Hz), 7.26(1H,s), 7.38(2H,dd,J=8.8,8.8Hz), 7.47(1H,d,J=8.8Hz,1H), 7.76(1H,d,J=2.0Hz,1H), 8.02(2H,dd,J=5.5,8.8Hz), 10.62(2H,brs), 11.95(1H,s).

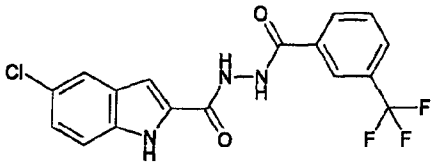
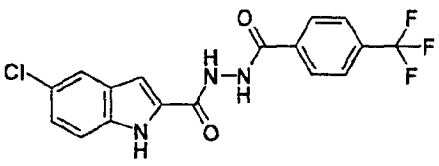
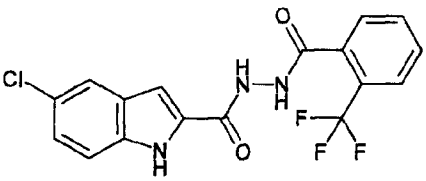
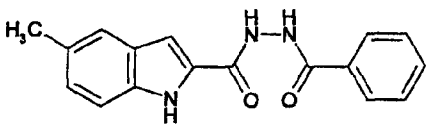
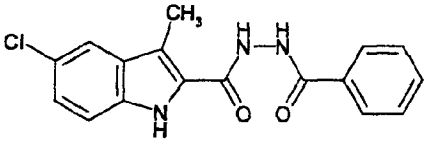
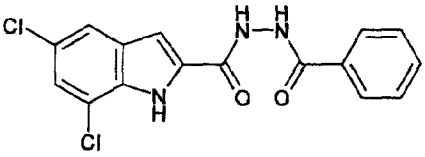
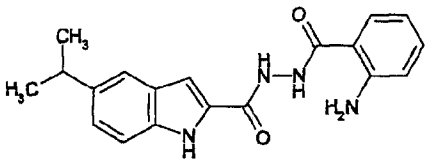
1-30		7.22(1H,dd,J=2.1,8.8Hz), 7.26(1H,s), 7.47(1H,d,J=8.8Hz), 7.76(1H,d,J=2.1Hz), 7.80(1H,dd,J=7.8,7.8Hz), 7.99(1H,d,J=7.8Hz), 8.25(1H,d,J=7.8Hz), 8.28(1H,s,), 10.79(2H,brs), 11.94(1H,brs).
1-31		7.23(1H,dd,J=2.0,8.7Hz), 7.27(1H,s), 7.47(1H,d,J=8.7Hz), 7.76(1H,d,J=2.0Hz), 7.93(2H,d,J=8.3Hz), 8.14(2H,d,J=8.3Hz), 10.76(2H,brs), 11.94(1H,brs).
1-32		7,23(1H,dd,J=2.2,8.8Hz), 7.28(1H,s), 7.47(1H,d,J=8.8Hz), 7.71-7.87(5H,m), 10.50(1H,brs), 10.71(1H,brs), 11.94(1H,brs).

Table-5

Ex.	Structural formula	^{1}H-NMR(δ,300MHz,DMSO-d6)
1-33		2.38(3H,s), 7.05(1H,d,J=8.4Hz), 7.18(1H,s), 7.35(1H,d,J=8.4Hz), 7.43(1H,s,), 7.51-7.64(3H,m), 7.95(2H,d,J=9.0Hz), 10.47(2H,brs), 11.57(1H,s).
1-34		2.54(3H,s), 7.23(1H,dd,J=2.1,8.7Hz), 7.44(1H,d,J=8.7Hz), 7.51-7.61(3H,m), 7.70(1H,d,J=2.1Hz), 7.95(2H,d,J=8.4Hz), 10.00(1H,brs), 10.57(1H,brs), 11.51(1H,s).
1-35		7.31(1H,s), 7.41(1H,d,J=1.8Hz), 7.51-7.64(3H,m,), 7.79(1H,d,J=1.8Hz), 7.94(2H,d,J=8.4Hz), 11.02(3H,brs).
1-36		(400MHz, DMSO-d6) 1.25(6H,d,J=6.8Hz), 2.96(1H,m) 6.47(2H,brs), 6.56(1H,m), 6.76(1H,m) 7.14(1H,m), 7.21(2H,m), 7.36(1H,m) 7.47(1H,s), 7.62(1H,m), 10.15(1H,brs), 10.37(1H,s), 11.58(1H,s).

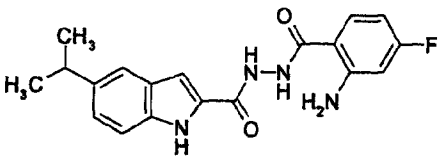
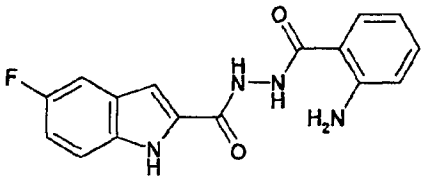
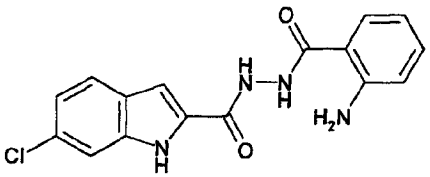
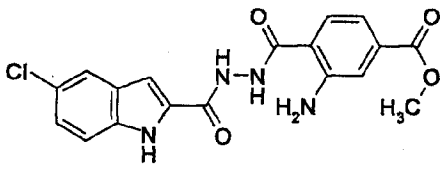
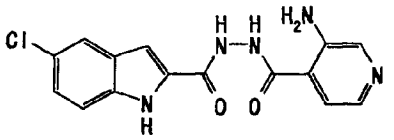
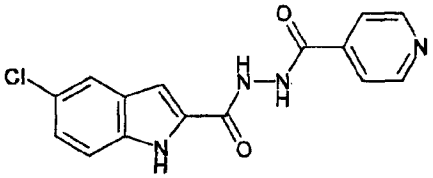
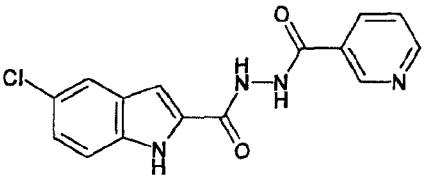
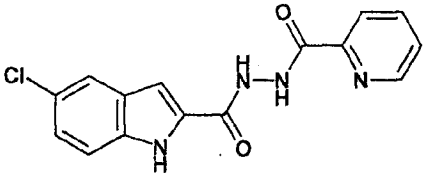
1-37		1.25(6H,d,J=7.0Hz), 2.96(1H,m), 6.38(1H,ddd,J=2.6, 8.8, 8.8Hz), 6.52(1H,dd,J=2.6, 12Hz), 6.78(2H,brs), 7.13(1H,dd,J=1.3, 8.4Hz), 7.20(1H,s), 7.37(1H,d,J=8.4Hz), 7.47(1H,s), 7.69(1H,dd,J=6.6, 8.8Hz), 10.17(1H,s), 10.35(1H,s), 11.56(1H,s).
1-38		6.47(2H,brs), 6.56(1H,dd,J=7.6, 7.6Hz), 6.75(1H,d,J=7.6Hz), 7.08(1H,ddd,J=2.5, 9.3, 9.3Hz), 7.19-7.26(2H,m), 7.43-7.47(2H,m), 7.63(1H,d,J=6.9Hz), 10.21(1H,brs), 10.46(1H,s), 11.84(1H,s).
1-39		6.47(2H,brs), 6.56(1H,dd,J=7.5, 7.5Hz), 6.75(1H,d,J=7.5Hz), 7.09(1H,dd,J=1.9, 8.6Hz), 7.21(1H,m), 7.29(1H,s), 7.46(1H,d,J=1.9Hz), 7.63(1H,d,J=6.8Hz), 7.70(1H,d,J=8.6Hz), 10.21(1H,brs), 10.48(1H,s), 11.88(1H,s).
1-40		3.85(3H,s), 6.65(2H,brs), 7.11(1H,dd,J=1.6, 8.2Hz), 7.21-7.26(2H,m), 7.42-7.48(2H,m), 7.71(1H,d,J=8.2Hz), 7.76(1H,d,J=2.0Hz), 10.42(1H,brs), 10.58(1H,s), 11.96(1H,s).

Table-6

Ex.	Structural formula	^{1}H-NMR (δ、300MHz,DMSO-d6)
1-41		6.54(2H,brs), 7,21-7.25(2H,m), 7.45-7.49(2H,m), 7.76-7.79(2H,m), 8.21(1H,s), 10.61(2H,m), 11.67(1H,s).
1-42		7.23(1H,dd,J=1.9,8.7Hz), 7.27(1H,s), 7.47(1H,d,J=8.7Hz), 7.77(1H,d,J=1.9Hz), 7.85(2H,d,J=6.0Hz), 8.81(2H,d,J=6.0Hz), 10.81(2H,brs), 11.97(1H,s).
1-43		7.23(1H,d,J=1.9,8.8Hz), 7.27(1H,s), 7.47(1H,d,J=8.8Hz), 7.59(1H,dd,J=4.8,7.9Hz), 7.77(1H,d,J=1.9Hz), 8.29(1H,d,J=7.9Hz), 8.8.0(1H,dd,J=1.6,4.8Hz), 9.10(1H,d,J=1.6Hz), 10.75(2H,brs), 11.97(1H,s).
1-44		7.22(1H,dd,J=2.0,8.7Hz), 7.26(1H,s), 7.47(1H,d,J=8.7Hz), 7.68(1H,m), 7.76(1H,d,J=2.0Hz), 8.05-8.10(2H,m), 8.72(1H,d,J=4.6Hz), 10.65(1H,brs), 10.71(1H,s), 11.94(1H,s).

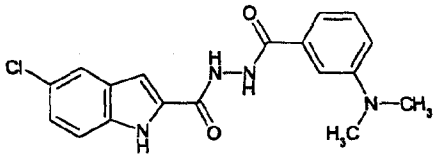
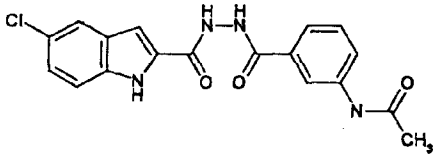
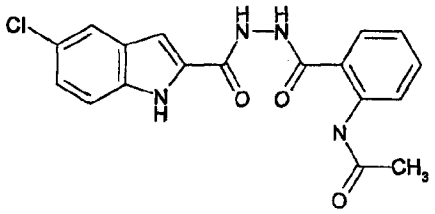
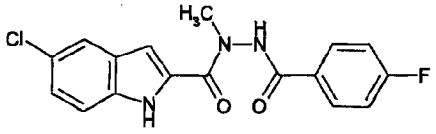
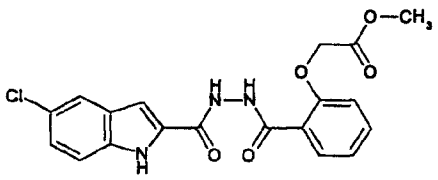
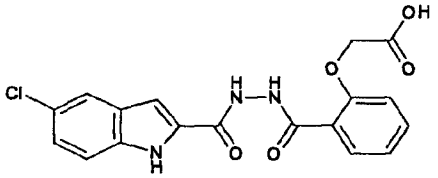
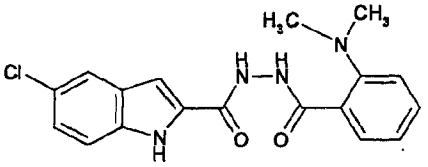
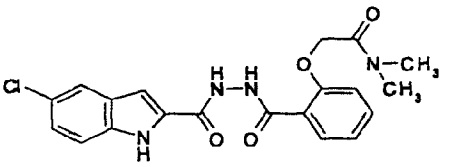
1-45		2.96(6H,s), 6.93(1H,dd,J=1.8,8.1Hz), 7.08-7.24(4H,m), 7.31(1H,dd,J=8.1,8.1Hz), 7.47(1H,d,J=8.1Hz), 7.75(1H,d,J=1.8Hz), 10.47(2H,brs), 11.90(1H,brs).
1-46		2.07(3H,s), 7.24(1H,dd,J=2.0,8.7Hz), 7.26(1H,s), 7.42-7.48(2H,m), 7.60(1H,d,J=7.9Hz), 7.76(1H,d,J=2.0Hz), 7.84(1H,d,J=7.9Hz), 8.10(1H,s), 10.14(1H,s,), 10.52(1H,s), 10.61(1H,s), 11.95(1H,s).
1-47		2.47(3H,s), 7.27(1H,dd,J=2.0,8.8Hz), 7.37(1H,s), 7.49(1H,d,J=8.8Hz), 7.56(1H,dd,J=7.3,7.3Hz), 7.70(1H,d,J=7.3Hz), 7.82(1H,d,J=2.0Hz,), 7.87(1H,dd,J=7.3,7.3Hz), 8.15(1H,d,J=7.3Hz), 11.30-11.93(3H,brs), 12.11(1H,brs).
1-48		3.29(3H,s), 6.88(1H,s), 6.88(1H,s), 7.17(1H,dd,J=1.8,8.9Hz), 7.36-7.44(3H,m), 7.61(1H,d,J=1.8Hz), 7.98-8.03(2H,m), 11.44(1H,brs), 11.83(1H,brs).

Table-7

Ex.	Structural formula	^{1}H-NMR (δ,300MHz,DMSO-d6)
1-49		3.74(3H,s), 5.04(2H,s), 7.13-7.27(4H,m), 7.47(1H,d,J=8.8Hz), 7.54(1H,ddd,J=1.8,7.9,7.9Hz), 7.75(1H,d,J=1.8Hz), 7.90(1H,dd,J=1.8,7.9Hz), 10.20(1H,s), 10.73(1H,s), 11.92(1H,s).
1-50		4.93(2H,s), 7.12-7.28(4H,m), 7.47(1H,d,J=8.8Hz), 7.54 (1H,dd,J=7.9,7.9Hz), 7.76(1H,d,J=1.6Hz), 7.92(1H,dd,J=1.5,7.9Hz), 10.31(1H,s), 10.73(1H,s), 11.94(1H,s), 13.37(1H,brs).
1-51		2.79(6H,s), 7.03-7.13(3H,m), 7.19(1H,d,J=8.1Hz), 7.39(1H,d,J=8.1Hz), 7.41(1H,m), 7.63(1H,d,J=1.8Hz), 7.74(1H,dd,J=1.5,8.1Hz), 11.00-12.00(3H,brs).
1-52		2.87(3H,s), 3.03(5H,s), 5.11(2H,s), 7.20-7.06(4H.m), 7.42(1H,d,J=8.4Hz), 7.49(1H,d,J=7.8Hz), 7.65(1H,s), 7.97(1H,d,J=7.8Hz), 11.28(2H,brs), 11.65(1H,brs).

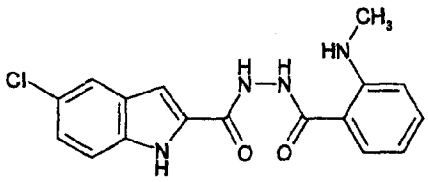
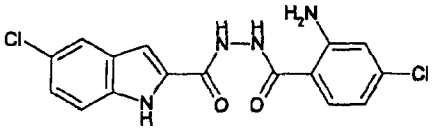
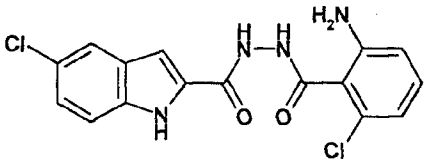
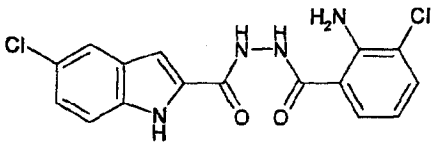
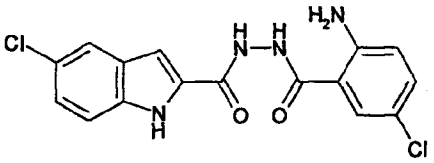
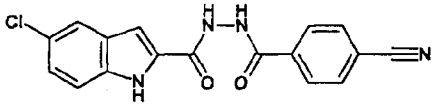
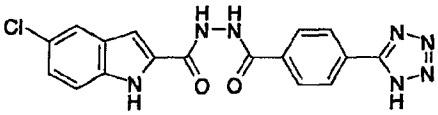
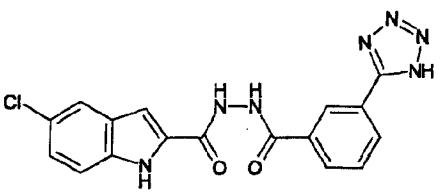
1-53		2.80(3H,d,J=5.1Hz), 6.61(1H,d,J=6.6,8.4Hz), 6.69(1H,d,J=8.4Hz), 7.22(1H,d,J=1.4,8.4Hz), 7.25(1H,d,J=1.4Hz), 7.37(1H,dd,J=6.6,8.4Hz), 7.46(1H,d,J=8.4Hz), 7.53(1H,q,J=5.1Hz), 7.68(1H,d,J=6.6Hz,), 7.75(1H,d,J=1.4Hz), 10.27(1H,s), 10.50(1H,s), 11.93(1H,s).
1-54		6.59(1H,dd,J=1.8,8.5Hz), 6.72(2H,brs), 6.83(1H,d,J=1.8Hz), 7.22(1H,dd,J=1.8,8.5Hz), 7.23(1H,d,J=1.8Hz), 7.46(1H,d,J=8.5Hz), 7.63(1H,d,J=8.5Hz), 7.75(1H,d,J=1.8Hz), 10.29(1H,s), 10.50(1H,s), 11.93(1H,s).
1-55		6.04(2H,brs), 6.60(1H,d,J=8.1Hz), 6.66(1H,d,J=8.1Hz), 7.10(1H,dd,J=8.1,8.1Hz), 7.24(1H,dd,J=1.8,8.6Hz), 7.29(1H,s), 7.46(1H,d,J=8.6Hz), 7.77(1H,d,J=1.8Hz), 10.45(1H,s), 10.95(1H,s), 12.03(1H,s).
1-56		6.54(2H,brs), 6.65(1H,dd,J=8.1,8.1Hz), 7.22(1H,dd,J=1.6,8.1Hz), 7.26(1H,d,J=1.6Hz), 7.46(1H,d,J=8.1Hz), 7.46(1H,d,J=8.1Hz), 7.63(1H,d,J=8.1Hz), 7.76(1H,d,J=1.6Hz), 10.43(1H,s), 10.59(1H,s), 11.96(1H,s).

Table-8

Ex.	Structural formula	^{1}H-NMR (δ,300MHz,DMSO-d6)
1-57		6.62(2H,brs), 6.79(1H,d,J=8.8Hz), 7.20-7.27(3H,m), 7.46(1H,d,J=8.8Hz), 7.68(1H,d,J=1.9Hz), 7.76(1H,d,J=1.9Hz), 10.24-10.46(2H,brs), 10.54(1H,brs).
1-58		7.23(1H,dd,J=1.8,8.7Hz), 7.27(1H,d,J=1.8Hz), 7.47(1H,d,J=8.7Hz), 7.77(1H,d,J=1.8Hz), 8.05(2H,d,J=8.6Hz), 8.10(2H,d,J=8.6Hz), 10.78(2H,brs), 11.98(1H,s).
1-59		7.23(1H,dd,J=2.0,8.7Hz), 7.28(1H,s), 7.48(1H,d,J=8.7Hz), 7.77(1H,s), 8.14(2H,d,J=8.4Hz), 8.21(2H,d,J=8.4Hz), 10.70(1H,s), 10.74(1H,s), 11.96(1H,s).
1-60		7.23(1H,dd,J=1.8,8.4Hz), 7.29(1H,d,J=1.8Hz), 7.48(1H,d,J=8.4Hz), 7.77(1H,d,J=1.8Hz), 7.80(1H,dd,J=8.0,8.0Hz), 8.14(1H,d,J=8.0Hz), 8.28(1H,d,J=8.0Hz), 8.65(1H,s), 10.72(1H,s), 10.80(1H,s), 11.97(1H,s).

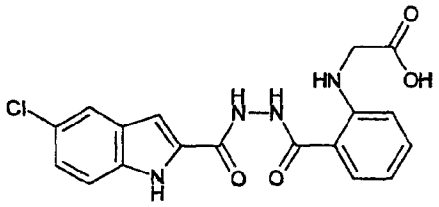
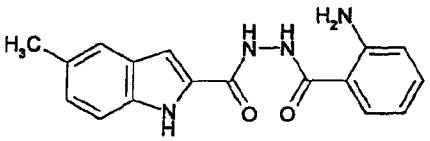
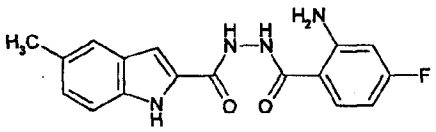
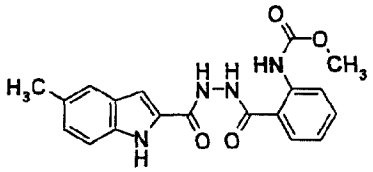
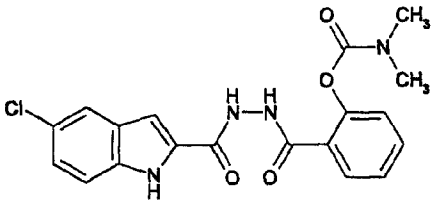
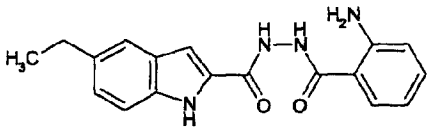
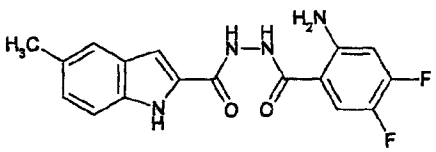
1-61		3.94(2H,s), 6.60-6.68(2H,m), 7.22(1H,dd,J=2.0,8.7Hz), 7.26(1H,d,J=2.0Hz), 7.35(1H,dd,J=7.6,7.6Hz), 7.46(1H,d,J=8.7Hz), 7.73(1H,d,J=7.6Hz), 7.76(1H,d,J=2.0Hz), 8.00(1H,brs), 10.31(1H,s), 10.51(1H,s), 11.94(1H,s), 12.77(1H,brs).
1-62		2.38(3H,s), 6.45(2H,brs), 6.56(1H,dd,J=7.0,7.0Hz), 6.75(1H,d,J=7.0Hz), 7.05(1H,d,J=8.3Hz), 7.18(1H,s), 7.20(1H,dd,J=7.0,7.0Hz), 7.34(1H,d,J=8.3Hz), 7.43(1H,s), 7.62(1H,d,J=7.0Hz), 10.16(1H,brs), 10.33(1H,s), 11.57(1H,s).
1-63		2.38(3H,s), 6.38(1H,m), 6.52(1H,dd,J=2.6,11.7Hz), 6.78(2H,brs), 7.04(1H,dd,J=1.5,8.3Hz), 7.17(1H,d,J=1.5Hz), 7.34(1H,d,J=8.3Hz), 7.42(1H,s), 7.69(1H,dd,J=6.8,8.6Hz), 10.18(1H,s), 10.33(1H,s), 11.57(1H,s).
1-64		2.38(3H,s), 3.69(3H,s), 7.06(1H,d,J=8.4Hz), 7.18(1H,s), 7.18(1H,m), 7.35(1H,d,J=8.4Hz), 7.44(1H,s), 7.59(1H,dd,J=7.3,8.4Hz), 7.83(1H,d,J=7.8Hz), 8.24 (1H,d,J=8.4Hz), 10.40(1H,s), 10.56(1H,s), 10.72(1H,s), 11.64(1H,s).

Table-9

Ex.	Structural formula	^{1}H-NMR (δ, 300MHz, DMSO-d6)
1-65		2.90(3H,s), 3.06(3H,s), 7.20-7.27(3H,m), 7.35(1H,dd,J=7.7,7.7Hz), 7.47(1H,d,J=8.8Hz), 7.55(1H,dd,J=7.7,7.7Hz), 7.65(1H,d,J=7.7Hz), 7.76(1H,s), 10.24(1H,s), 10.62(1H,s), 11.92(1H,s).
1-66		1.23(3H,t,J=7.7Hz), 2.67(2H,q,J=7.7Hz), 6.45(2H,brs), 6.56(1H,dd,J=7.3,7.3Hz), 6.75(1H,d,J=7.3Hz), 7.08(1H,dd,J=1.5,8.4Hz), 7.20(1H,s), 7.20(1H,dd,J=7.3,7.3Hz), 7.36(1H,d,J=8.4Hz), 7.45(1H,s), 7.63(1H,d,J=7.3Hz), 10.16(1H,brs), 10.34(1H,s), 11.57(1H,s).
1-67		2.38(3H,s), 6.69(2H,brs), 6.73(1H,dd,J=7.3,13.3Hz), 7.05(1H,d,J=8.4Hz), 7.17(1H,s), 7.34(1H,d,J=8.4Hz), 7.43(1H,s), 7.71(1H,dd,J=9.0,12.0Hz), 10.24(1H,brs), 10.39(1H,s), 11.60(1H,s).

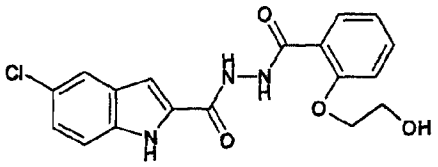
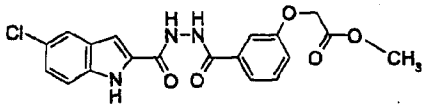
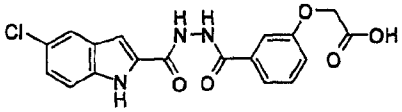
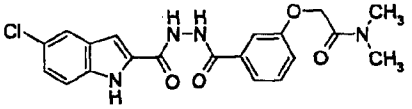
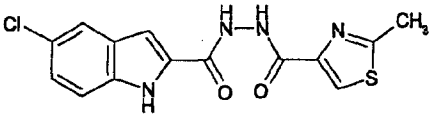
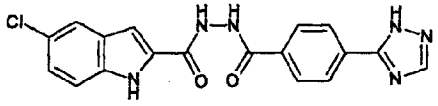
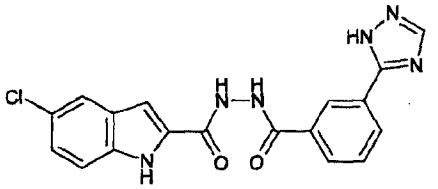
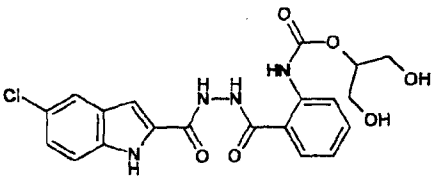
1-68		3.82(2H,td,J=4.8,5.4Hz), 4.22(2H,t,J=4.8Hz), 5.08(1H,t,J=5.4Hz), 7.11(1H,dd,J=7.4,7.4Hz), 7.20-7.25(2H,m), 7.28(1H,d,J=1.8Hz), 7.47(1H,d,J=8.7Hz), 7.55(1H,m), 7.75(1H,d,J=1.8Hz), 7.84(1H,dd,J=2.0,7.4Hz), 10.14(1H,s), 10.81(1H,s), 11.93(1H,s).
1-69		3.72(3H,s), 4.90(2H,s), 7.18-7.26(3H,m), 7.43-7.58(4H,m), 7.76(1H,s), 10.54(1H,s), 10.62(1H,s), 11.94(1H,s).
1-70		4.76(2H,s), 7.14-7.26(3H,m), 7.42-7.56(4H,m), 7.76(1H,d,J=1.8Hz), 10.54(1H,brs), 10.61(1H,brs), 11.94(1H,s).
1-71		2.86(3H,s), 3.02(3H,s), 4.90(2H,s), 7.13-7.26(3H,m), 7.40-7.54(4H,m), 7.76(1H,d,J=1.8Hz), 10.51(1H,s), 10.61(1H,s), 11.94(1H,s).
1-72		2.75(3H,s), 7.21(1H,dd,J=2.0,8.8Hz), 7.25(1H,d,J=2.0Hz), 7.46(1H,d,J=8.8Hz), 7.75(1H,d,J=2.0Hz), 8.26(1H,s), 10.34(1H,s), 10.59(1H,s), 11.92(1H,s).

Table-10

Ex.	Structural formula	^{1}H-NMR (δ,300MHz,DMSO-d6)
1-73		7.23(1H,dd,J=1.9,8.8Hz), 7.28(1H,s), 7.48(1H,d,J=8.8Hz), 7.65(1H,m), 7.77(1H,d,J=1.9Hz), 7.99(1H,d,J=6.6Hz), 8.24(1H,d,J=7.2Hz), 8.62(1H,s), 8.69(1H,brs), 10.66(1H,s), 10.71(1H,s), 11.95(1H,s), 14.21(1H,brs).
1-74		7.23(1H,dd,J=2.0,8.8Hz), 7.28(1H,s), 7.48(1H,d,J=8.8Hz), 7.77(1H,s), 8.06(2H,d,J=7.8Hz), 8.18(2H,d,J=7.8Hz), 8.70(1H,brs), 10.65(2H,brs), 11.95(1H,brs), 14.25(1H,brs).
1-75		3.46-3.60(4H,m), 4.71(1H,m), 4.82(2H,d,J=5.7Hz), 7.15-7.26(3H,m), 7.47(1H,d,J=8.8Hz), 7.60(1H,dd,J=7.3,7.3Hz), 7.77(1H,d,J=1.5Hz), 7.87(1H,d,J=7.3Hz), 8.31(1H,d,J=7.3Hz), 10.43(1H,s), 10.70(1H,s), 10.80(1H,s), 11.97(1H,s).

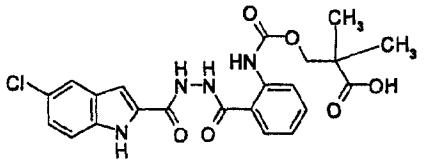
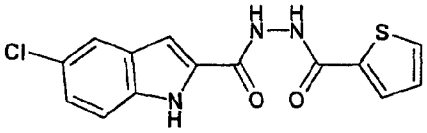
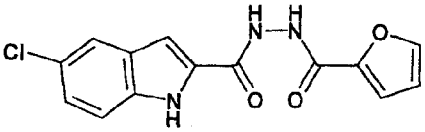
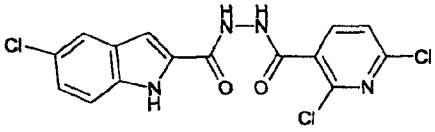
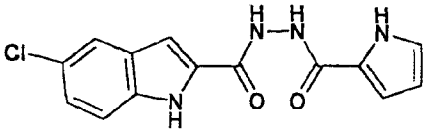
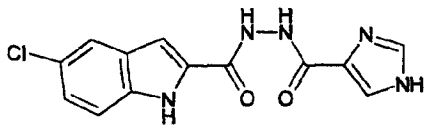
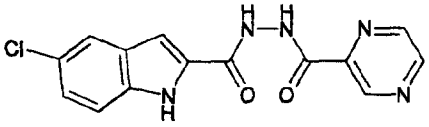
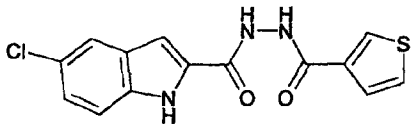
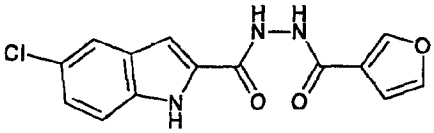
1-76		1.14(6H,s), 4.12(2H,s), 7.16-7.27(3H,m), 7.47(1H,d,J=8.7Hz), 7.60(1H,dd,J=8.0,8.0Hz), 7.77(1H,s), 7.88(1H,d,J=8.0Hz), 8.25(1H,d,J=8.0Hz), 10.52(1H,s)10.70(1H,s), 10.79(1H,s), 11.95(1H,s), 12.38(1H,brs).
1-77		7.21-7.25(2H,m), 7.25(1H,s), 7.47(1H,d,J=8.8Hz), 7.76(1H,d,J=1.8Hz), 7.87-7.91(2H,m), 10.58(1H,s), 10.63(1H,s), 11.96(1H,s).
1-78		6.71(1H,dd,J=3.5Hz,1.7Hz), 7.22(1H,dd,J=1.9,8.8Hz), 7.24(1H,s), 7.29(1H,d,J=3.5Hz), 7.46(1H,d,J=8.8Hz), 7.76(1H,d,J=1.9Hz), 7.94(1H,d,J=1.7Hz), 10.45(1H,s), 10.57(1H,s), 11.95(1H,s).
1-79		7.23(1H,dd,J=2.0,8.7Hz), 7.27(1H,s), 7.47(1H,d,J=8.7Hz), 7.75(1H,d,J=8.0Hz), 7.77(1H,s), 8.06(1H,d,J=8.0Hz), 10.73(1H,brs), 10.86(1H,brs), 11.97(1H,s).
1-80		6.16(1H,brs), 6.95(2H,brs), 7.22(1H,dd,J=2.0,8.8Hz), 7.25(1H,s), 7.46(1H,d,J=8.8Hz), 7.75(1H,s), 10.06(1H,s), 10.48(1H,s), 11.66(1H,brs), 11.95(1H,s).

Table-11

Ex.	Structural formula	^{1}H-NMR(δ,300MHz,DMSO-d6)
1-81		7.21(1H,dd,J=2.1,8.8Hz), 7.24(1H,s), 7.46(1H,d,J=8.8Hz), 7.74(1H,d,J=2.1Hz), 7.77(1H,s), 7.80(1H,s), 9.91(1H,brs), 10.45(1H,s), 11.90(1H,s), 12.59(1H,brs).
1-82		7.22(1H,dd,J=2.1,8.7Hz), 7.27(1H,s), 7.47(1H,d,J=8.7Hz), 7.76(1H,d,J=2.1Hz), 8.81(1H,dd,J=1.2,2.4Hz), 8.95(1H,d,J=2.4Hz), 9.23(1H,d,J=1.2Hz), 10.69(1H,s), 10.90(1H,s), 11.94(1H,brs).
1-83		7.22(1H,dd,J=2.0,8.8Hz), 7.25(1H,s), 7.46(1H,d,J=8.8Hz), 7.59(1H,dd,J=1.1,5.0Hz), 7.68(1H,dd,J=2.9,5.0Hz), 7.76(1H,d,J=2.0Hz), 8.29(1H,dd,J=1.1,2.9Hz), 10.41(1H,brs), 10.60(1H,brs), 11.95(1H,s).
1-84		6.95(1H,d,J=1.4Hz), 7.22(1H,dd,J=2.0,8.8Hz), 7.24(1H,s), 7.46(1H,d,J=8.8Hz), 7.76(1H,d,J=2.0Hz), 7.81(1H,m), 8.33(1H,s), 10.30(1H,s), 10.57(1H,s), 11.95(1H,s).

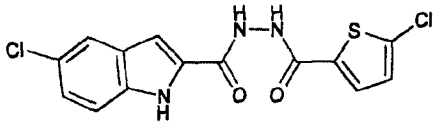
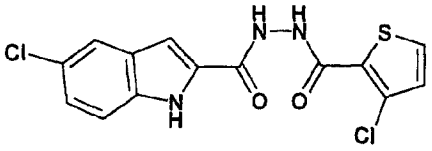
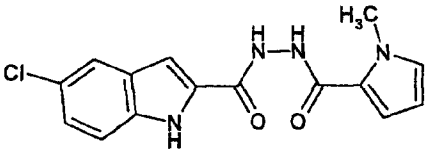
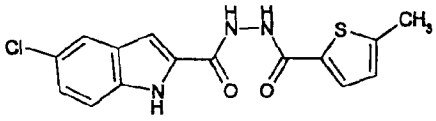
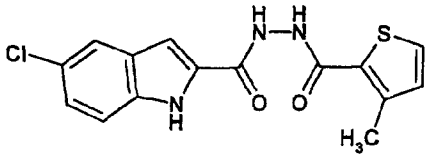
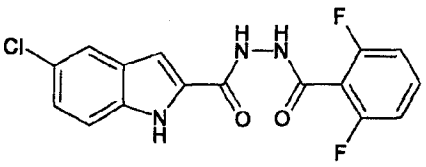
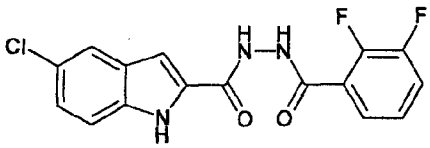
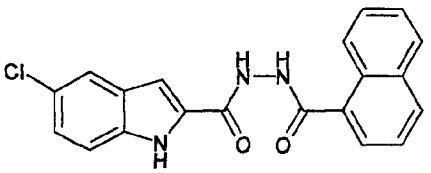
1-85		7.23(1H,dd,J=1.9,8.7Hz), 7.24(1H,s), 7.29(1H,d,J=4.1Hz), 7.46(1H,d,J=8.7Hz), 7.76(1H,d,J=1.9Hz), 7.79(1H,d,J=4.1Hz), 10.67(1H,s), 10.70(1H,s), 11.97(1H,s).
1-86		7.21-7.24(3H,m), 7.47(1H,d,J=8.7Hz), 7.76(1H,d,J=1.9H), 7.93(1H,d,J=5.3Hz), 10.27(1H,s), 10.70(1H,s,), 11.95(1H,s).
1-87		3.85(3H,s), 6.08(1H,dd,J=2.6,3.7Hz), 6.97(1H,d,J=3.7Hz), 7.00(1H,d,J=2.6Hz), 7.21(1H,dd,J=2.3,8.7Hz), 7.23(1H,s), 7.46(1H,d,J=8.7Hz), 7.75(1H,d,J=2.3Hz), 9.99(1H,s), 10.42(1H,s), 11.91(1H,s).
1-88		2.50(3H,s), 6.92(1H,d,J=3.0Hz), 7.22(1H,dd,J=2.0,9.0Hz), 7.24(1H,s), 7.46(1H,d,J=9.0Hz), 7.71(1H,d,J=3.0Hz), 7.75(1H,d,J=2.0Hz), 10.44(1H,s), 10.56(1H,s), 11.93(1H,s).

Table-12

Ex.	Structural formula	^{1}H-NMR(δ,300MHz,DMSO-d6)
1-89		2.48(3H,s), 7.23(1H,d,J=5.0Hz), 7.22(1H,dd,J=1.8,8.7Hz), 7.29(1H,s), 7.47(1H,d,J=8.7Hz), 7.67(1H,d,J=5.0Hz), 7.75(1H,d,J=1.8Hz), 10.05(1H,s), 10.57(1H,s), 11.92(1H,s).
1-90		7.21-7.34(4H,m), 7.47(1H,d,J=9.0Hz), 7.61(1H,m), 7.76(1H,d,J=2.1Hz), 10.73(1H,s), 10.80(1H,s), 11.94(1H,s).
1-91		7.21-7.26(2H,m), 7.37(1H,m), 7.47(1H,d,J=8.7Hz), 7.47(1H,m), 7.65(1H,m), 7.76(1H,d,J=1.8Hz), 10.55(1H,brs), 10.74(1H,brs), 11.94(1,s).
1-92		7.24(1H,dd,J=2.0,8.7Hz), 7.29(1H,s), 7.48(1H,d,J=8.7Hz), 7.60-7.64(3H,m), 7.73(1h,d,J=6.0Hz), 7.78(1H,d,J=2.0H), 8.02(1h,m), 8.10(1H,d,J=8.1Hz), 8.47(1H,m), 10.52(1H,s), 10.77(1H,s), 12.05(1H,s).

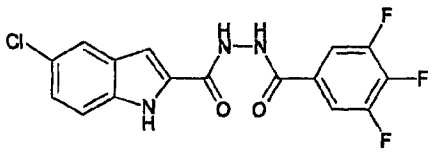
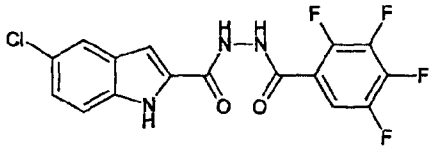
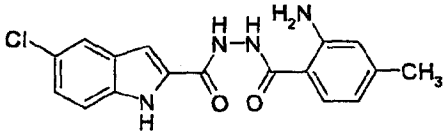
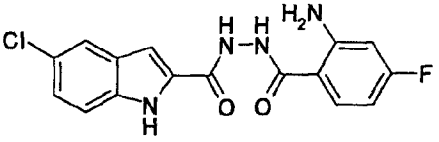
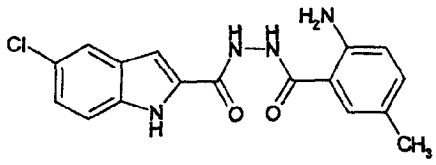
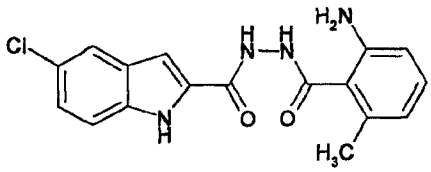
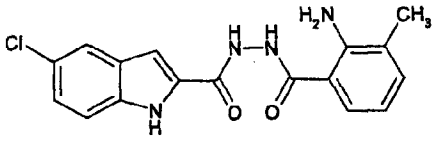
1-93		7.23(1H,dd,J=2.0,8.8Hz), 7.26(1H,s), 7.47(1H,d,J=2.0Hz), 7.77(1H,d,J=8.8Hz), 7.99(2H,m), 10.74(1H,s), 10.78(1H,s), 11.98(1H,s).
1-94		7.23(1H,dd,J=2.0,8.8Hz), 7.26(1H,s), 7.47(1H,d,J=8.8Hz), 7.69(1H,m), 7.76(1H,d,J=2.0Hz), 10.68(1H,brs), 10.80(1H,brs), 11.97(1H,s).
1-95		2.20(3H,s), 6.38(1H,d,J=8.6Hz), 6.45(2H,brs), 6.55(1H,s), 7.22(1H,dd,J=1.8,8.6Hz), 7.24(1H,s), 7.46(1H,d,J=8.6Hz), 7.55(1H,d,J=8.6Hz), 7.75(1H,s), 10.11(1H,brs), 10.43(1H,s), 11.91(1H,s).
1-96		6.39(1H,m), 6.52(1H,dd,J=2.6,11.9Hz), 6.8(2H,brs), 7.22(1H,dd,J=2.0,8.8Hz), 7.25(1H,s), 7.46(1H,d,J=8.8Hz), 7.70(1H,dd,J=6.7,8.7Hz), 7.75(1H,d,J=2.0Hz), 10.23(1H,brs), 10.49(1H,brs), 11.94(1H,s).

Table-13

Ex.	Structural formula	^{1}H-NMR(δ,300MHz,DMSO-d6)
1-97		2.19(3H,s), 6.24(2H,brs), 6.67(1H,d,J=8.3Hz), 7.05(1H,d,J=8.3Hz), 7.22(1H,dd,J=2.0,8.7Hz), 7.24(1H,s), 7.46(1H,d,J=8.7Hz), 7.46(1H,s), 7.75(1H,d,J=2.0Hz), 10.17(1H,brs), 10.48(1H,s), 11.93(1H,s).
1-98		2.23(3H,s), 5.56(2H,brs), 6.40(1H,d,J=7.4Hz), 6.54(1H,d,J=8.0Hz), 6.99(1H,dd,J=7.4,8.0Hz), 7.23(1H,dd,J=2.0,8.8Hz), 7.26(1H,s), 7.46(1H,d,J=8.8Hz), 7.77(1H,d,J=2.0Hz), 10.23(1H,s), 10.76(1H,s), 12.03(1H,s)
1-99		2.11(3H,s), 6.26(2H,brs), 6.54(1H,dd,J=7.1,7.6Hz), 7.15(1H,d,J=7.1Hz), 7.22(1H,dd,J=2.0,8.7Hz), 7.25(1H,s), 7.46(1H,d,J=8.7Hz), 7.52(1H,d,J=7.6Hz), 7.76(1H,d,J=2.0Hz), 10.22(1H,s), 10.51(1H,s), 11.95(1H,s).

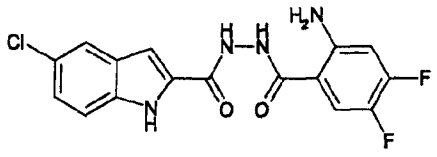
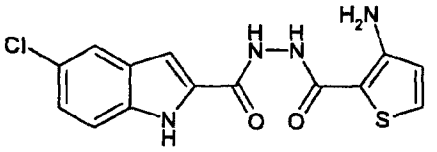
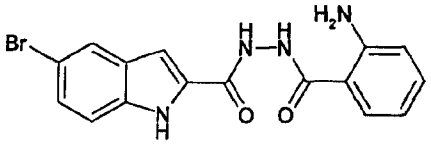
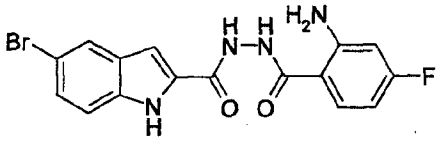
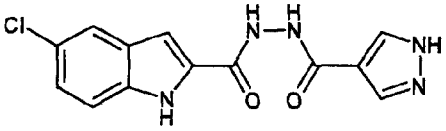
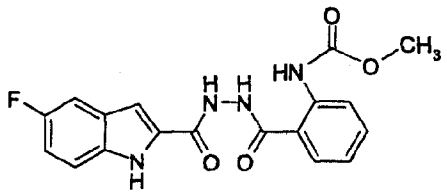
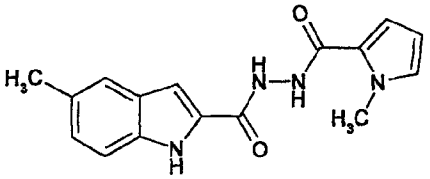
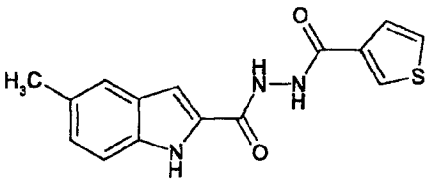
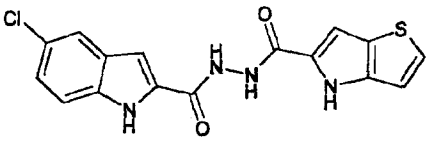
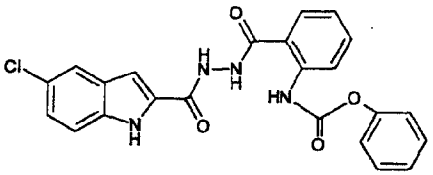
1-100		6.70(2H,brs), 6.73(1H,dd,J=7.2,13.5Hz), 7.22(1H,dd,J=2.2,8.8Hz), 7.25(1H,s), 7.46(1H,d,J=8.8Hz), 7.71(1H,dd,J=9.0,12.0Hz), 7.75(1H,s), 10.27(1H,brs,1H), 10.53(1H,s), 11.93(1H,s).
1-101		6.57(2H,br), 6.63(1H,d,J=5.3Hz), 7.22(1H,dd,J=2.0,8.9Hz), 7.23(1H,s), 7.45(1H,d,J=8.9Hz), 7.47(1H,d,J=5.3Hz), 7.75(1H,d,J=2.0Hz), 9.54(1H,brs), 10.39(1H,brs), 11.92(1H,s).
1-102		6.47(2H,brs), 6.56(1H,dd,J=7.4,7.4,Hz), 6.75(1H,d,J=7.4Hz), 7.21(1H,dd,J=7.4,7.4Hz), 7.25(1H,s), 7.33(1H,dd,J=8.7,1.8Hz), 7.42(1H,d,J=8.7Hz), 7.63(1H,d,J=7.4Hz), 7.90(1H,d,J=1.8Hz), 10.21(1H,brs), 10.50(1H,s), 11.96(1H,s).
1-103		6.39(1H,m), 6.52(1H,dd,J=2.6,11.9Hz), 6.80(2H,brs), 7.25(1H,s), 7.33(1H,dd,J=1.8,8.7Hz,1H), 7.42(1H,d,J=8.7Hz), 7.70(1H,dd,J=7.2,8.7Hz), 7.90(1H,d,J=1.8Hz), 10.23(1H,s), 10.50(1H,s), 11.95(1H,s).
1-104		7.22(1H,dd,J=2.0,8.8Hz), 7.25(1H,s), 7.46(1H,d,J=8.8Hz), 7.75(1H,d,J=2.0Hz), 8.01(1H,brs), 8.32(1H,brs), 10.16(1H,s), 10.52(1H,s), 11.95(1H,s,), 13.29(1H,brs).

Table-14

Ex.	Structural formula	^{1}H-NMR(δ,300MHz,DMSO-d6)
1-105		3.69(3H,s), 7.09(1H,m), 7.18(1H,m), 7.26(1H,s), 7.44-7.48(2H,m), 7.591(1H,m), 7.83(1H,d,J=6.6Hz), 8.23(1H,d,J=8.4Hz), 10.39(1H,s), 10.68(1H,s), 10.76(1H,s), 11.89(1H,s).
1-106		2.38(3H,s), 3.85(3H,s), 6.08(1H,m)6.96-7.06(3H,m), 7.16(1H,s)7.34(1H,d,J=8.4Hz), 7.42(1H,s)9.95(1H,s), 10.27(1H,s), 11.55(1H,s).
1-107		2.38(3H,s), 7.05(1H,dd,J=1.5, 8.2Hz) 7.18(1H,d,J=1.5Hz), 7.34(1H,d,J=8.2Hz), 7.43(1H,s), 7.59(1H,dd,J=1.2, 4.9Hz), 7.67(1H,dd,J=3.0, 4.9Hz), 8.29(1H,dd,J=1.2, 3.0Hz), 10.35(1H,s), 10.43(1H,s), 11.58(1H,s).
1-108		6.99(1H,d,J=5.3Hz), 7.21-7.26(3H,m), 7.45-7.48(2H,m), 7.77(1H,d,J=1.9Hz), 10.32(1H,s), 10.57(1H,s), 11.91(1H,s), 11.98(1H,s).
1-109		7.21-7.28(6H,m), 7.41-7.48(3H,m), 7.63(1H,m), 7.77(1H,s), 7.90(1H,d,J=7.5Hz), 8.23(1H,d,J=8.4Hz), 10.77(1H,s), 10.87(2H,s), 11.99(1H,s).

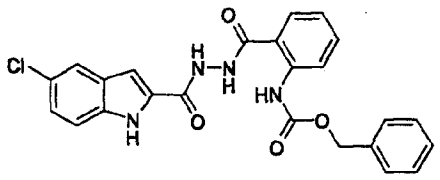
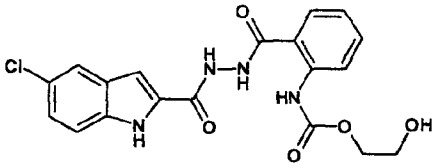
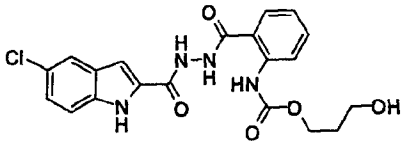
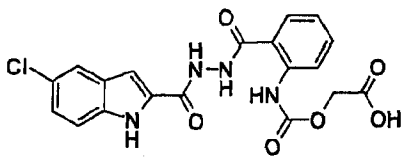
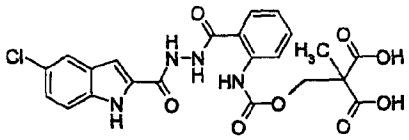
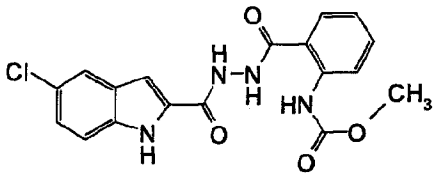
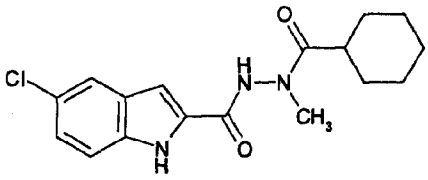
1-110		5.17(2H,s), 7.17-7.25(3H,m), 7.31-7.48(6H,m), 7.60(1H,m), 7.76(1H,d,J=1.8Hz), 7.86(1H,d,J=6.6Hz), 8.26(1H,d,J=7.8Hz), 10.54(1H,s), 10.69(1H,s), 10.79(1H,s), 11.97(1H,s).
1-111		3.60(2H,m), 4.11(2H,t,J=4.9Hz), 4.86(1H,t,J=5.5Hz), 7.16-7.26(3H,m), 7.47(1H,d,J=8.7Hz), 7.59(1H,m), 7.77(1H,s), 7.85(1H,d,J=7.5Hz), 8.27(1H,d,J=8.4Hz), 10.42(1H,s), 10.70(1H,s), 10.79(1H,s), 11.98(1H,s).
1-112		1.76(2H,m), 3.47(2H,m), 4.16(2H,t,J=6.5Hz), 4.54(1H,t,J=5.1Hz), 7.15-7.26(3H,m), 7.47(1H,d,J=8.7Hz), 7.59(1H,m), 7.78(1H,d,J=1.9Hz), 7.85(1H,d,J=6.8Hz), 8.26(1H,d,J=8.1Hz), 10.43(1H,s), 10.71(1H,s), 10.79(1H,s), 11.98(1H,s).

Table-15

Ex.	Structural formula	^{1}H-NMR(δ,300MHz,DMSO-d6)
1-113		4.61(2H,s), 7.19-7.26(2H,m), 7.47(1H,d,J=8.7Hz), 7.61(1H,m), 7.77(1H,s), 7.87(1H,d,J=6.8Hz), 8.22(1H,d,J=8.3Hz), 10.60(1H,s), 10.73(1H,s), 10.82(1H,s), 12.00(1H,s), 13.05(1H,brs).
1-114		1.35(3H,s), 4.40(2H,s), 7.17-7.27(3H,m), 7.47(1H,d,J=8.8Hz), 7.60(1H,m), 7.77(1H,d,J=1.9Hz), 7.89(1H,d,J=6.9Hz), 8.24(1H,d,J=8.3Hz), 10.56(1H,s), 10.72(1H,s), 10.81(1H,s), 11.97(1H,s), 13.10(2H,brs).
1-115		3.69(3H,s), 7.16-7.27(3H,m), 7.47(1H,d,J=9.0Hz), 7.59(1H,t,J=7.8Hz), 7.78-7.84(2H,m), 10.39(1H,s), 10.72(1H,s), 10.77(1H,s), 11.99(1H,s).
1-116		1.13(3H,m), 1.32(2H,m), 1.56-1.67(5H,m), 2.50(1H,m), 3.08(3H,s), 7.21-7.26(2H,m), 7.46(1H,d,J=8.4Hz), 7.78(1H,d,J=1.8Hz), 11.02(1H,s), 12.05(1H,s).

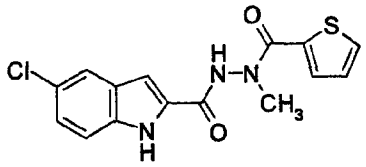
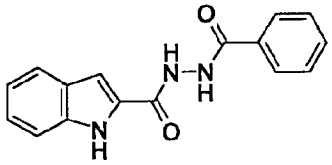
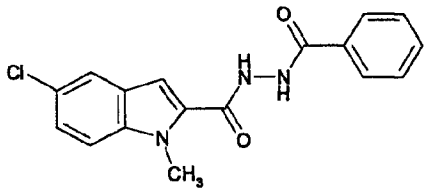
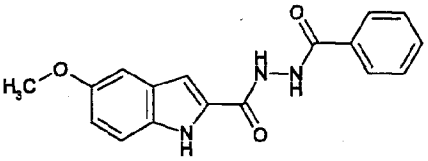
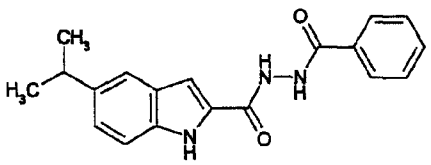
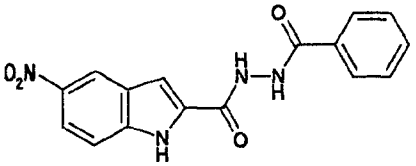
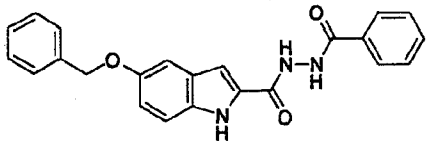
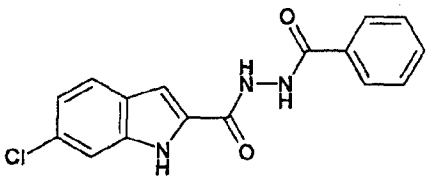
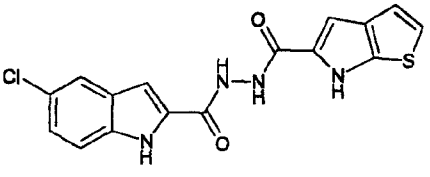
1-117		3.27(3H,s), 7.09(1H,dd,J=3.9, 5.0Hz), 7.23-7.30(2H,m), 7.45(1H,d,J=8.8Hz), 7.74(1H,m), 7.78-7.82(2H,m), 11.43(1H,s), 12.07(1H,s).
1-118		3.09(1H,dd,J=7.6,16Hz), 3.36(1H,m), 4.37(1H,m), 5.99(1H,d,J=3.2Hz), 6.57-6.61(2H,m), 6.95(1H,m), 7.03(1H,d,J=7.1Hz), 7.47-7.60(3H,m), 7.87(2H,m), 9.93(1H,brs), 10.37(1H,brs).
1-119		4.00(3H,s), 7.24(1H,s), 7.32(1H,dd,J=2.1, 8.7Hz), 7.51-7.64(4H,m), 7.79(1H,d,J=2.1Hz), 7.93-7.95(2H,m), 10.54(1H,s), 10.57(1H,s),
1-120		3.78(3H,s), 6.87(1H,dd,J=2.4, 9.0Hz), 7.13(1H,d,J=2.1Hz), 7.20(1H,s), 7.35(1H,d,J=9.0Hz), 7.51-7.64(3H,m), 7.93-7.96(2H,m), 10.47(1H,s), 10.50(1H,s), 11.56(1H,s),

Table-16

Ex.	Structural formula	^{1}H-NMR(δ,300MHz,DMSO-d6)
1-121		1.25(6H,d,J=6.9Hz), 2.96(1H,m), 7.14(1H,dd,J=1.5, 8.5Hz), 7.22(1H,d,J=1.5Hz), 7.38(1H,d,J=8.5Hz), 7.48-7.64(4H,m), 7.93-7.96(2H,m), 10.50(1H,s), 10.51(1H,s), 11.59(1H,s),
1-122		7.52-7.65(5H,m), 7.94(2H,m), 8.12(1H,dd,J=2.2, 9.1Hz), 8.78(1H,d,J=2.2Hz), 10.64(1H,brs), 10.80(1H,brs), 12.49(1H,brs),
1-123		5.12(2H,s), 6.96(1H,dd,J=2.5, 8.7Hz), 7.21(2H,m), 7.30-7.42(4H,m), 7.47-7.64(5H,m), 7.95(2H,m), 10.47(1H,s), 10.50(1H,s), 11.58(1H,s),
1-124		7.09(1H,dd,J=1.9, 8.6Hz), 7.30(1H,s), 7.47(1H,s), 7.52-7.64(3H,m), 7.71(1H,d,J=8.6Hz), 7.95(2H,m), 10.56(1H,s), 10.62(1H,s), 11.89(1H,s),
1-125		7.05-7.10(2H,m), 7.19-7.26(3H,m), 7.47(1H,d,J=8.7Hz), 7.77(1H,d,J=1.9Hz), 10.29(1H,s), 10.56(1H,s), 11.98(1H,s), 12.10(1H,s),

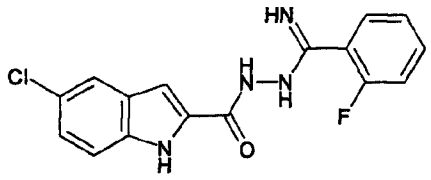
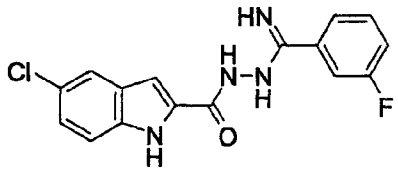
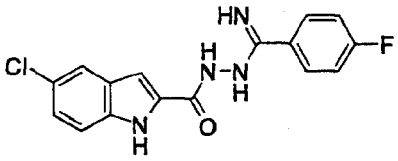
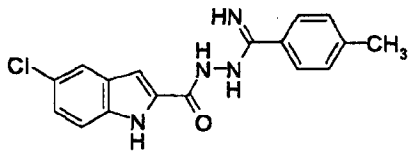
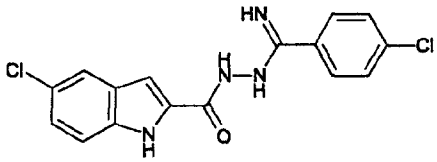
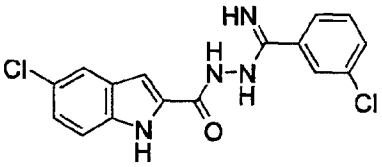
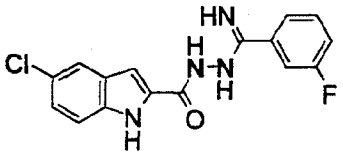
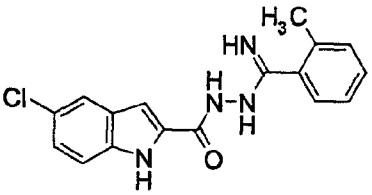
1-126		6.86(2H,brs), 7.18(1H,dd,J=1.8,9.0Hz), 7.26-7.31(3H,m), 7.43-7.50(2H,m), 7.60-7.72(2H,m), 10.10(1H,brs), 11.83(1H,brs),
1-127		6.89(2H,brs), 7.18(1H,dd,J=1.8, 8.7Hz), 7.27-7.34(2H,m), 7.44-7.52(2H,m), 7.64-7.75(3H,m), 10.12(1H,brs), 11.84(1H,brs).
1-128		6.84(2H,brs), 7.19(1H,d,J=8.6Hz), 7.26-7.32(3H,m), 7.45(1H,m), 7.72(1H,s), 7.92(2H,m), 10.09(1H,brs), 11.84(1H,brs).

Table-17

Ex.	Structural formula	^{1}H-NMR(δ,300MHz,DMSO-d6)
1-129		2.36(3H,s), 6.75(2H,brs), 7.17-7.27(4H,m), 7.44(1H,m), 7.71(1H,s), 7.77(2H,d,J=8.2Hz), 10.05(1H,brs), 11.82(1H,brs).
1-130		6.88(2H,brs), 7.19(1H,dd,J=1.9, 8.7Hz), 7.26(1H,s), 7.45(1H,d,J=8.7Hz), 7.53(2H,d,J=8.5Hz), 7.72(1H,s), 7.89(2H,d,J=8.5Hz), 10.11(1H,brs), 11.85(1H,brs).
1-131		6.93(2H,brs), 7.19(1H,d,J=8.7Hz), 7.27(1H,s), 7.44-7.53(3H,m), 7.72(1H,d,J=1.7Hz), 7.84(1H,d,J=7.4Hz), 7.91(1H,s), 10.13(1H,brs), 11.86(1H,brs).
1-132		6.88(2H,brs), 7.18(1H,d,J=8.4Hz), 7.27(1H,s), 7.42-7.55(5H,m), 7.72(1H,s), 10.07(1H,brs), 11.83(1H,brs).
1-133		2.41(3H,s), 6.76(2H,brs), 7.16-7.45(7H,m), 7.70(1H,s), 10.06(1H,brs), 11.78(1H,brs).

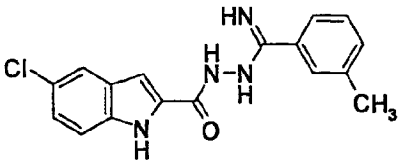
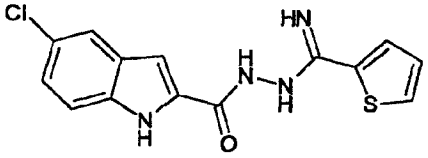
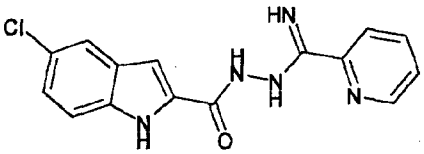
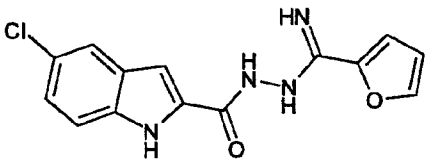
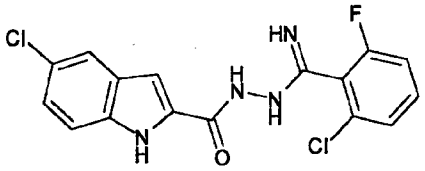
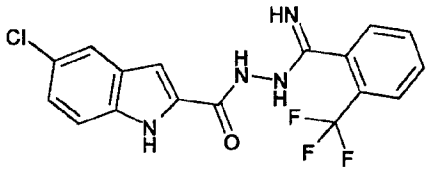
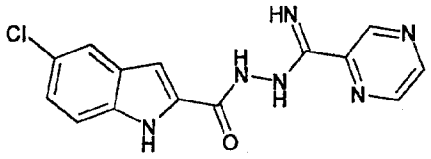
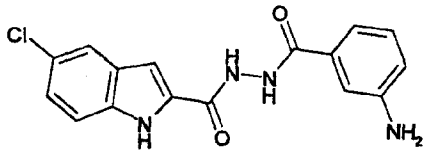
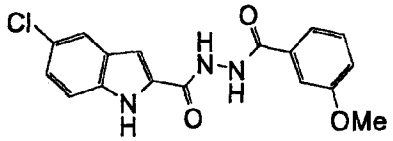
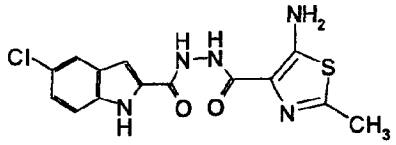
1-134		2.37(3H,s), 6.80(2H,brs), 7.18(1H,dd,J=1.8, 8.7Hz), 7.25-7.36(3H,m), 7.45(1H,d,J=8.7Hz), 7.63-7.71(3H,m), 10.07(1H,brs), 11.81(1H,brs).
1-135		6.86(2H,brs), 7.11(1H,m), 7.17-7.22(2H,m), 7.45(1H,d,J=8.7Hz), 7.59(1H,d,J=5.4Hz), 7.66(1H,d,J=3.0Hz), 7.71(1H,d,J=1.8Hz), 10.12(1H,brs), 11.80(1H,brs).
1-136		6.89-7.06(2H,m), 7.20(1H,d,J=9.0Hz), 7.30(1H,s), 7.45-7.53(2H,m), 7.73(1H,s), 7.94(1H,m), 8.20(1H,d,J=7.8Hz), 8.62(1H,d,J=4.5Hz), 10.24(1H,brs), 11.86(1H,brs).

Table-18

Ex.	Structural formula	^{1}H-NMR(δ,300MHz,DMSO-d6)
1-137		6.62(1H,s), 6.75(2H,brs), 7.00(1H,s), 7.20(2H,m), 7.45(1H,d,J=9.0Hz), 7.71(1H,s), 7.81(1H,s), 10.08(1H,brs), 11.84(1H,brs).
1-138		7.02(2H,brs), 7.18(1H,d,J=8.1Hz), 7.28-7.36(2H,m), 7.40-7.53(3H,m), 7.73(1H,s), 10.12(1H,brs), 11.85(1H,brs).
1-139		6.90(2H,brs), 7.18(1H,d,J=8.4Hz), 7.27(1H,s), 7.44(1H,d,J=8.8Hz), 7.58-7.82(5H,m), 10.09(1H,brs), 11.82(1H,brs).
1-140		7.12(2H,brs), 7.21(1H,dd,J=1.8, 8.4Hz), 7.33(1H,s), 7.47(1H,d,J=8.4Hz), 7.75(1H,s), 8.69(1H,s), 8.74(1H,d,J=2.4Hz), 9.35(1H,s), 10.34(1H,brs), 11.89(1H,brs).

1-141		5.30(2H,brs), 6.75(1H,d,J=7.0Hz), 7.04-7.24(4H,m), 7.24(1H,s), 7.46(1H,d,J=8.8Hz), 7.75(1H,d,J=1.8Hz), 10.30(1H,brs), 10.50(1H,brs), 11.90(1H,s).
1-142		3.82(3H,s), 6.78(1H,m), 7.04(1H,m), 7.17-7.25(1H,m), 7.36-7.47(3H,m), 7.7.1(1H,s), 10.07(1H,s), 11.81(1H,s).
1-143		2.47(3H,s), 7.11(2H,m), 7.19-7.22(2H,m), 9.58(1H,s), 10.39(1H,s), 11.90(1H,s).

Example 2

N-(1,2,3,4-tetrahydro-2,4-dioxoquinazolin-3-yl)-5-chloro-1H-indole-2-carboxamide

2-Aminobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide obtained in Example 1-2 (329 mg) and sodium hydrogencarbonate (168 mg) were suspended in a mixed solvent of THF (10 ml) and water (3 ml) and cooled in an ice bath. Triphosgene (168 mg) was added in divided portions over 20 min. This reaction solution was stirred at room temperature for 1 hr. The separated organic layer was washed 3 times with half-saturated brine and dried over anhydrous sodium sulfate. This solution was filtered and concentrated to give an oily substance. Thereto was added chloroform to give the title compound (317 mg, yield 89%) as crystals (see Table 19).

Example 2-2

N-(1,2,3,4-tetrahydro-2,4-dioxobenzo[e][1,3]oxazin-3-yl)-5-chloro-1H-indole-2-carboxamide

In the same manner as in Example 1-2, the title compound was obtained from 2-hydroxybenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide obtained in Example 1-3 (see Table 19).

Example 2-3

N-(1,2,3,4-tetrahydro-4-oxo-2-thioxoquinazolin-3-yl)-5-chloro-1H-indole-2-carboxamide

2-Aminobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)-hydrazide obtained in Example 1-2 (1.31 g) was dissolved in THF (26 ml). Thiocarbonyldiimidazole (867 mg) was added and the mixture was stirred at room temperature for 2 hr. The reaction solvent was evaporated under reduced pressure and the obtained residue was dissolved in ethyl acetate. This solution was washed successively with water, aqueous hydrochloric acid (0.5N), saturated aqueous sodium hydrogen carbonate and water. This solution was dried over anhydrous sodium sulfate and filtrated. The filtrate was evaporated under reduced pressure

and the residue was crystallized from ethyl acetate and diethyl ether to give the title compound (910 mg, yield 61.3%) as pale-yellow crystals (see Table 19).

Example 2-4

5-chloro-1H-indole-2-carboxylic acid (2-methyl-4-oxo-4H-quinazolin-3-yl)-amide

2-Amino-benzoic acid 2-(5-chloro-1H-indole-2-carbonyl)-hydrazide obtained in Example 1-2 (90 mg) was dissolved in DMF (1 ml). To this solution were successively added methyl orthoacetate (3 ml) and methanesulfonic acid (0.05 ml) and the mixture was stirred at room temperature for 30 min. Water (2 ml) was added to the reaction mixture and extracted with ethyl acetate-THF (1:1) (50 ml). The organic layer was washed successively with water (2×20 ml) and saturated aqueous sodium chloride solution (20 ml), dried and concentrated under reduced pressure. The obtained solid was washed with ether in a slurry form to give the title compound (77 mg, yield 80%) as a colorless solid (see Table 19).

Example 2-5

5-chloro-1H-indole-2-carboxylic acid (4-oxo-4H-quinazolin-3-yl)-amide

2-Amino-benzoic acid 2-(5-chloro-1H-indole-2-carbonyl)-hydrazide obtained in Example 1-2 (87.1 mg) was suspended in formic acid (3 ml). The mixture was heated to 120°C and stirred for 6 hr. The reaction mixture was allowed to cool to room temperature and water (30 ml) was added. The mixture was extracted with ethyl acetate-THF (1:1) (50 ml). The organic layer was washed successively with saturated aqueous sodium hydrogen carbonate solution (30 ml) and saturated aqueous sodium chloride solution (30 ml), dried and concentrated under reduced pressure. The obtained solid was washed with MeOH in a slurry form to give the title compound (65 mg, yield 72%) as a colorless solid (see Table 19).

Example 2-6

5-chloro-1H-indole-2-carboxylic acid (4-oxo-1,4-dihydro-2H-quinazolin-3-yl)-amide

5-Chloro-1H-indole-2-carboxylic acid (4-oxo-4H-quinazolin-3-yl)amide obtained in Example 2-5 (44 mg) was dissolved in THF-MeOH (1:1) (16 ml). To this solution were successively added acetic acid (0.4 ml) and sodium cyanoborohydride (145 mg) and the mixture was heated to 85°C and stirred for 42 hr. Water (30 ml) was added to the reaction mixture and the mixture was extracted with ethyl acetate-THF (1:1) (80 ml). The organic layer was washed with saturated aqueous sodium chloride solution (30 ml), dried and concentrated under reduced pressure. The obtained solid was washed with ether in a slurry form to give the title compound (42 mg, yield 94%) as a colorless solid (see Table 19).

Example 2-7

5-chloro-1H-indole-2-carboxylic acid (2,5-dioxo-1,2,3,5-tetrahydro-benzo[e][1,4]diazepin-4-yl)-amide

2-Amino-benzoic acid 2-(5-chloro-1H-indole-2-carbonyl)-hydrazide obtained in Example 1-2 (203 mg) was dissolved in THF (25 ml). Pyridine (0.28 ml) was added to this solution and the mixture was cooled to 0°C. Acetyl chloride (0.054 ml) was added and the reaction mixture was heated to room temperature and stirred for 12 hr and 30 min. Water (50 ml) was added to the reaction mixture and the mixture was extracted with THF-ethyl acetate (1:1) (100 ml). The organic layer was washed successively with 10% aqueous citric acid solution (30 ml), water (30 ml) and saturated aqueous sodium chloride solution (30 ml), dried and concentrated under reduced pressure. The obtained solid was washed with ether in a slurry form.

This solid was dissolved in DMF (7 ml). To this solution were successively added potassium carbonate (225 mg) and sodium iodide (catalytic amount) and the mixture was heated to

80°C and stirred for 2 hr. The reaction mixture was allowed to cool to room temperature and water (30 ml) was added. The mixture was extracted with THF-ethyl acetate (1:1) (100 ml). The organic layer was washed with saturated aqueous sodium chloride solution (30 ml), dried and concentrated under reduced pressure. The obtained solid was washed with THF in a slurry form to give the title compound (117 mg, yield 67%) as a colorless solid (see Table 19).

Example 2-8

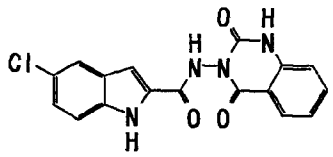
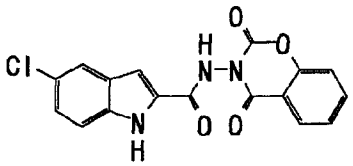
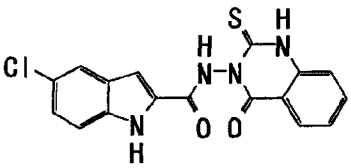
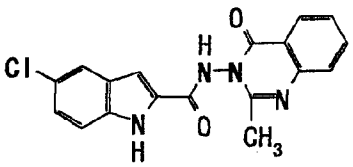
5-chloro-1H-indole-2-carboxylic acid (2,5-dioxo-2,3-dihydro-5H-benzo[e][1,4]oxazepin-4-yl)-amide

2-(Carboxymethyl)hydroxy-benzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide (131 mg) and HOBt·H_2O (85 mg) were dissolved in DMF (2.5 ml) and EDC (85 mg) was added. The mixture was stirred at room temperature for 16 hr. The reaction mixture was diluted with THF-ethyl acetate (1:1) (80 ml) and washed successively with water (30 ml), 10% aqueous citric acid solution (30 ml), water (30 ml) and saturated aqueous sodium chloride solution (30 ml). This solution was dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The obtained solid was washed with ether in a slurry form to give the title compound (89 mg, yield 58%) as a colorless solid (see Table 19).

Examples 2-9 to 2-31

In the same manner as in Examples 2 to 2-8, the compounds of Examples 2-9 to 2-31 were obtained. The obtained compounds are shown in Tables 19-22.

Table-19

Ex.	Structural formula	^{1}H-NMR(δ,300MHz,DMSO-d6)
2		7.24-7.35(5H,m,), 7.49(1H,d,J=8.8Hz), 7.74-7,82(2H,m), 8.00(1H,d,J=7.9Hz), 11.27(1H,s), 11.78(1H,s), 12.02(1H,s).
2-2		7.27(dd,J=1.8,8.2Hz), 7.43(1H,d,J=1.8Hz), 7.49(1H,d,J=8.2Hz), 7.54(1H,dd,J=8.2,8.2Hz), 7.58(1H,d,J=8.2Hz), 7.82(1H,d,J=1.8Hz), 7.94(1H,dd,J=8.2,8.2Hz), 8.09(1H,dd,J=1.8,8.2Hz), 11.71(1H,s), 12.07(1H,s).
2-3		7.24-7.27(1H,m,), 7.38-7.49(4H,m), 7.82-7,85(2H,m), 8.03(1H,d,J=7.9Hz), 11.61(1H,s), 12.03(1H,s), 13.27(1H,s).
2-4		2.48(3H,s), 7.28(1H,dd,J=1.8,8.7Hz), 7.41(1H,d,J=1.8Hz), 7.50(1H,d,J=8.7Hz), 7.57(1H,dd,J=6.8,6.8Hz), 7.71(1H,d,J=7.7Hz), 7.85(1H,d,J=1.8Hz), 7.90(1H,ddd,J=1.5,6.8,7.7Hz), 8.14(1H,dd,J=1.5,6.8Hz), 11.75(1H,s), 12.14(1H,s).

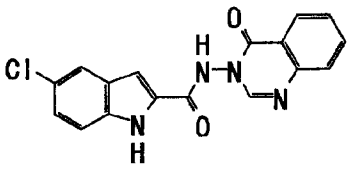
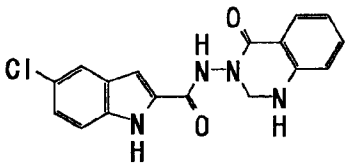
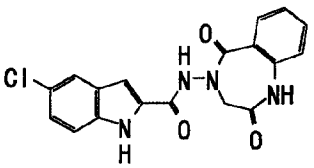
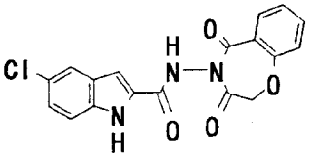
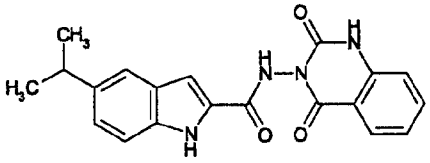
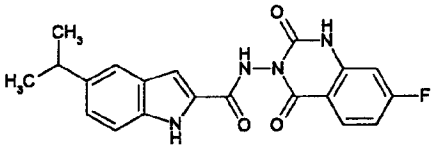
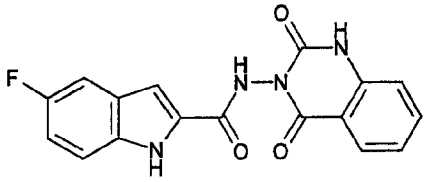
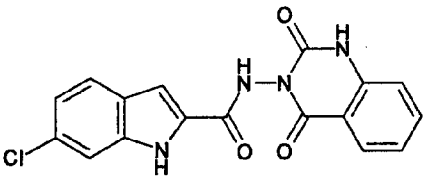
2-5		7.28(1H,dd,J=1.2,8.3Hz), 7.40(1H,d,J=1.7Hz), 7.50(1H,d,J=8.1Hz), 7.65(1H,ddd,J=1.2,8.3,8.3Hz), 7.80(1H,d,J=8.1Hz), 7.85(1H,d,J=1.7Hz), 7.94(1H,ddd,J=1.2,8.3,8.3Hz), 8.24(1H,dd,J=1.2,8.3Hz), 8.49(1H,s), 11.97(1H,s), 12.14(1H,s).
2-6		4.84(2H,d,J=1.8Hz), 6.76-6.83(2H,m), 7.02(1H,brs), 7.21-7.25(2H,m), 7.35(1H,m), 7.47(1H,d,J=8.8Hz), 7.70(1H,d,J=7.7Hz), 7.77(1H,d,J=1.8Hz), 10.96(1H,s), 11.98(1H,s).
2-7		4.15(2H,s), 7.18-7.31(4H,m), 7.48(1H,d,J=8.8Hz), 7.59(1H,ddd,J=1.5,8.1,8.1Hz), 7.78(1H,d,J=2.2Hz), 7.82(1H,dd,J=1.5,8.1Hz), 10.64(1H,s), 11.38(1H,s), 11.98(1H,s).
2-8		5.10(1H,d,J=15.8Hz), 5.16(1H,d,J=15.8Hz), 7.25(1H,dd,J=2.0,8.7Hz), 7.28-7.32(2H,m), 7.38(1H,dd,J=8.0,8.0Hz), 7.48(1H,d,J=8.7Hz), 7.72(1H,dd,J=8.0,8.0Hz), 7.81(1H,d,J=2.0Hz), 8.12(1H,dd,J=1.7,8.0Hz), 11.27(1H,s), 11.99(1H,s).

Table-20

Ex.	Structural formula	^{1}H-NMR(δ,300MHz,DMSO-d6)
2-9		1.26(6H,d,J=6.9Hz), 2.98(1H,m), 7.17(1H,d,J=8.7Hz), 7.29(3H,m), 7.39(1H,d,J=8.4Hz), 7.52(1H,s), 7.76(1H,dd,J=7.6, 7.6Hz), 8.00(1H,d,J=7.6Hz), 11.10(1H,s), 11.66(1H,s), 11.76(1H,s)
2-10		1.26(6H,d,J=6.9Hz), 2.97(1H,m), 7.01(1H,dd,J=2.3, 9.8Hz), 7.12-7.19(2H,m), 7.30(1H,s), 7.39(1H,d,J=8.5Hz), 7.52(1H,s), 8.07(1H,m), 11.14(1H,s), 11.68(1H,s), 11.92(1H,s).
2-11		7.12(1H,m), 7.27-7.36(3H,m), 7.45-7.54(2H,m), 7.76(1H,m), 8.00(1H,d,J=7.8Hz), 11.24(1H,s), 11.80(1H,s), 11.94(1H,s).
2-12		7.13(1H,m), 7.26-7.32(2H,m), 7.39(1H,s), 7.49(1H,s), 7.74-7.79(2H,m), 8.00(1H,d,J=7.7Hz), 11.25(1H,s), 11.79(1H,s), 11.96(1H,s).

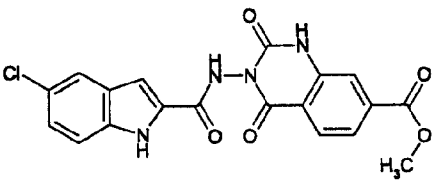
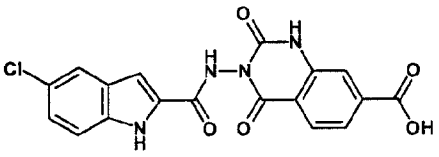
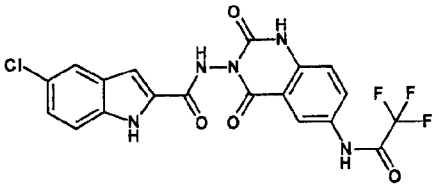
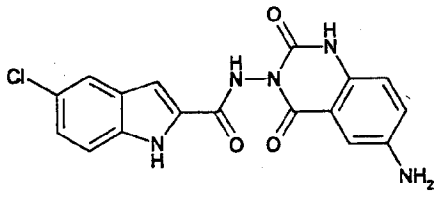
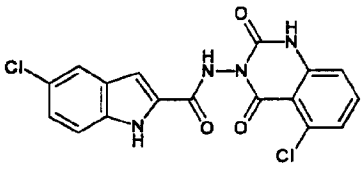
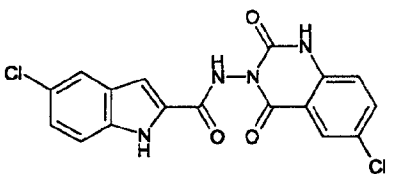
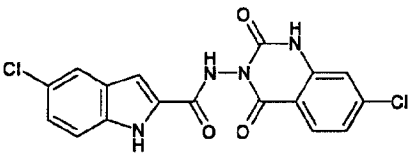
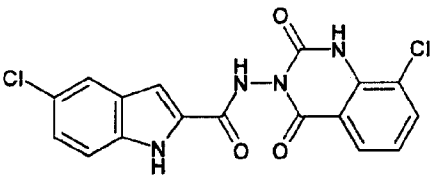
2-13		3.93(3H,s), 7.26(1H,dd,J=2.0, 8.8Hz), 7.37(1H,s), 7.49(1H,d,J=8.8Hz), 7.78-7.86(3H,m), 8.14(1H,d,J=8.0Hz), 11.35(1H,s), 12.00(1H,s), 12.04(1H,s).
2-14		7.26(1H,dd,J=2.1, 8.8Hz), 7.36(1H,d,J=1.5Hz), 7.49(1H,d,J=8.8Hz), 7.76-7.85(3H,m), 8.11(1H,d,J=8.2Hz), 11.35(1H,s), 11.99(1H,s), 12.05(1H,s), 13.58(1H,brs).
2-15		7.24-7.36(3H,m), 7.49(1H,d,J=8.7Hz), 7.82(1H,d,J=2.1Hz), 8.02(1H,dd,J=2.7,8.7Hz), 8.36(1H,d,J=2.7Hz), 11.30(1H,s), 11.48(1H,brs), 11.88(1H,brs), 12.03(1H,s).
2-16		5.31(2H,brs), 7.02(2H,m), 7.15(1H,d,J=2.0Hz), 7.25(1H,dd,J=2.0,8.7Hz), 7.32(1H,d,J=1.4Hz), 7.48(1H,d,J=8.7Hz), 7.81(1H,d,J=2.0Hz), 11.16(1H,s), 11.34(1H,s), 12.02(1H,s).

Table-21

Ex.	Structural formula	^{1}H-NMR(δ,300MHz,DMSO-d6)
2-17		7.23-7.27(2H,m), 7.34(1H,d,J=8.4Hz), 7.35(1H,s), 7.49(1H,d,J=8.4Hz), 7.68(1H,dd,J=8.4,8.4Hz), 7.82(1H,d,J=2.1Hz), 11.23(1H,s), 11.92(1H,s), 12.02(1H,s).
2-18		7.24-7.36(3H,m), 7.48(1H,d,J=8.8Hz), 7.80-7.84(2H,m), 7.95(1H,d,J=2.4Hz), 11.34(1H,brs), 11.96(1H,brs), 12.04(1H,s).
2-19		7.24-7.36(4H,m), 7.48(1H,d,J=8.4Hz), 7.81(1H,s), 8.01(1H,d,J=8.4Hz), 11.30(1H,s), 11.92(1H,s), 12.02(1H,s).
2-20		7.26(1H,dd,J=1.8,8.7Hz), 7.31(1H,dd,J=8.0,8.0Hz), 7.38(1H,d,J=1.8Hz), 7.49(1H,d,J=8.7Hz), 7.82(1H,d,J=1.8Hz), 7.92(1H,dd,J=1.3,8.0Hz), 8.01(1H,dd,J=1.3,8.0Hz), 11.37(2H,brs), 12.05(1H,s).

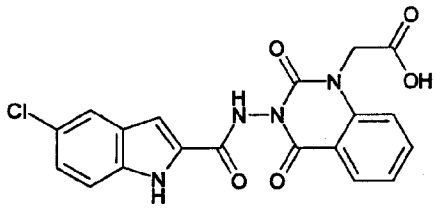
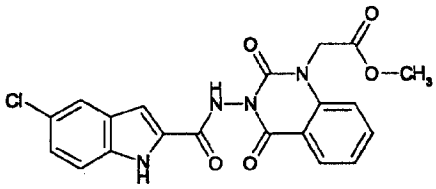
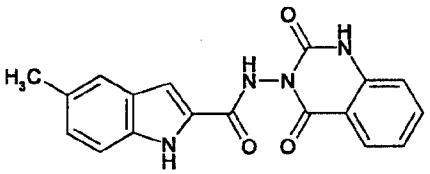
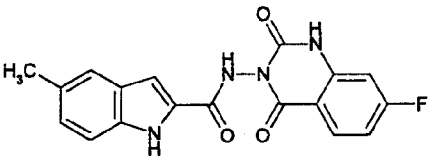
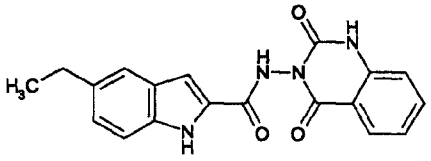
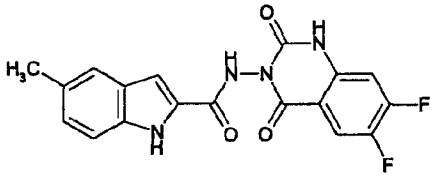
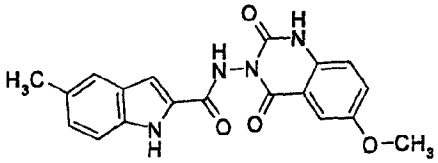
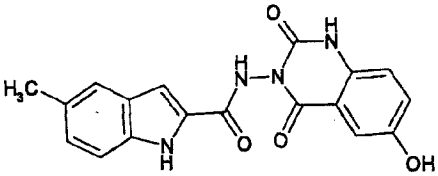
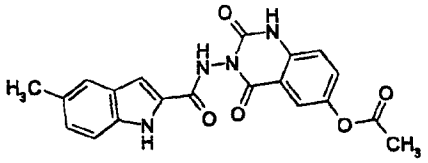
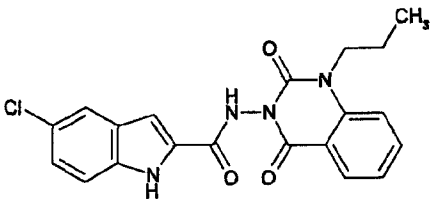
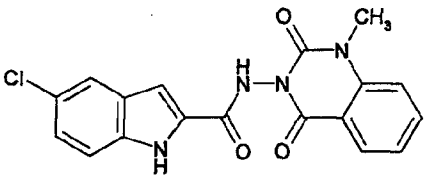
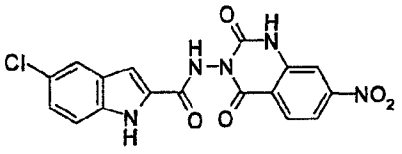
2-21		4.96(2H,s), 7.26(1H,dd,J=1.9,8.8Hz), 7.35(1H,d,J=1.9Hz), 7.40(1H,dd,J=7.9,7.9Hz), 7.49(1H,d,J=8.8Hz), 7.49(1H,d,J=7.9Hz), 7.82(1H,d,J=1.9Hz), 7.85(1H,m), 8.15(1H,dd,J=1.9, 7.9Hz), 11.43(1H,s), 12.03(1H,s), 13.30(1H,brs).
2-22		3.73(3H,s), 5.07(2H,s), 7.26(1H,dd,J=2.0,8.9Hz), 7.35(1H,d,J=2.0Hz), 7.41,(1H,dd,J=7.8,7.8Hz), 7.47-7.53(2H,m), 7.82(1H,d,J=2.0Hz), 7.85(1H,m), 8.15(1H,dd,J=1.5,7.8Hz), 11.44(1H,s), 12.03(1H,s).
2-23		2.39(3H,s), 7.08(1H,dd,J=1.5,8.1Hz), 7.26-7.31(3H,m), 7.37(1H,d,J=8.1Hz), 7.48(1H,s), 7.76(1H,ddd,J=1.5,8.1,8.1Hz), 8.00(1H,d,J=8.1Hz), 11.10(1H,s), 11.67(1H,s), 11.76(1H,s).
2-24		2.39(3H,s), 7.01(1H,dd,J=2.4,9.7Hz), 7.08(1H,d,J=8.4Hz), 7.15(1H,m), 7.26(1H,s), 7.37(1H,d,J=8.4Hz), 7.48(1H,s), 8.07(1H,dd,J=5.9,8.8Hz), 11.12(1H,s), 11.67(1H,s), 11.90(1H,s).

Table-22

Ex.	Structural formula	^{1}H-NMR(δ,300MHz,DMSO-d6)
2-25		1.24(1H,t,J=7.7Hz), 2.69(2H,q,J=7.7Hz), 7.12(1H,d,J=8.4Hz), 7.26-7.31(3H,m), 7.39(1H,d,J=8.4Hz), 7.50(1H,s), 7.75(1H,dd,J=7.3,7.3Hz), 8.00(1H,d,J=7.3Hz), 11.10(1H,s), 11.67(1H,s), 11.76(1H,s).
2-26		2.39(3H,s), 7.09(1H,d,J=8.7Hz), 7.22(1H,dd,J=6.6,11.1Hz), 7.27(1H,d,J=1.8Hz), 7.36(1H,d,J=8.7Hz), 7.48(1H,s), 8.00(1H,dd,J=8.4,10.2Hz), 11.16(1H,s), 11.68(1H,s), 11.94(1H,s).
2-27		2.39(3H,s), 3.83(3H,s), 7.08(1H,d,J=8.4Hz), 7.25(1H,m), 7.27(1H,s), 7.35-7.41(3H,m), 7.47(1H,s), 11.11(1H,s), 11.67(1H,s), 11.68(1H,s).
2-28		2.39(3H,s), 7.09(1H,m), 7.15(1H,s), 7.20-7.25(2H,m), 7.31(1H,d,J=3.0Hz), 7.36(1H,d,J=8.7Hz), 7.48(1H,s), 9.79(1H,s), 11.03(1H,s), 11.50(1H,s), 11.66(1H,s).

2-29		2.29(3H,s), 2.39(3H,s), 7.08(1H,d,J=8.7Hz), 7.27-7.38(3H,m), 7.48(1H,s), 7.55(1H,dd,J=2.7,8.7Hz), 7.74(1H,d,J=2.7Hz), 11.14(1H,s), 11.68(1H,s), 11.85(1H,s).
2-30		0.96(3H,t,J=7.3Hz), 1.70(2H,tq,7.3,7.3Hz), 4.14(2H,t,J=7.3Hz), 7.26(1H,dd,J=1.8,8.8Hz), 7.36(1H,s), 7.38(1H,m), 7.48(1H,d,J=8.8Hz), 7.62(1H,d,J=8.8Hz), 7.82(1H,s), 7.87(1H,m), 8.13(1H,d,J=6.6Hz), 11.38(1H,s), 12.02(1H,s).
2-31		3.60(3H,s), 7.26(1H,dd,J=1.8,8.4Hz), 7.37(1H,s), 7.40(1H,m), 7.49(1H,d,J=8.6Hz), 7.56(1H,d,J=8.6Hz), 7.82(1H,d,J=1.8Hz), 7.89(1H,ddd,J=1.8,8.4,8.4Hz), 8.12(1H,dd,1.8,8.4Hz), 11.37(1H,s), 12.02(1H,s).
2-32		7.26(1H,dd,J=2.0,8.7Hz), 7.38(1H,d,J=2.0Hz), 7.49(1H,d,J=8.7Hz), 7.82(1H,d,J=2.0), 8.03(1H,dd,J=2.0,8.7Hz), 8.05(1H,s), 8.25(1H,d,J=8.7Hz), 11.42(1H,s), 12.05(1H,s), 12.22(1H,s).

Example 3

N-(2,4-dioxo-perhydropyrimidin-3-yl)-5-chloro-1H-indole-2-carboxamide

a) tert-butyl {3-[2-(5-chloro-1H-indole-2-carbonyl)hydrazino]-3-oxopropyl}carbamate

In the same manner as in Example 1-2 and using N-(tert-butoxycarbonyl)-β-alanine instead of anthranilic acid, the title compound (yield 48%) was obtained.

^{1}H-NMR (δ, 300MHz,DMSO-d_6).

1.39(9H,s),2.37(2H,t,J=7.5Hz),3.19(2H,m),6.81(1H,m),7.19-7.23(2H,m),7.45(1H,d,J=8.7Hz),7.73(1H,m),9.97(1H,brs),11.83(1H,s).

b)N-(2,4-dioxo-perhydropyrimidin-3-yl)-5-chloro-1H-indole-2-carboxamide

tert-Butyl {3-[2-(5-chloro-1H-indole-2-carbonyl)hydrazino]-3-oxopropyl}carbamate obtained in Example 3 a) (577 mg) was dissolved in trifluoroacetic acid (6 ml) under ice-cooling. Trifluoroacetic acid was evaporated under reduced pressure to give a solid residue. This residue was dissolved in THF (3 ml) and triethylamine (0.31 ml) was added. To this solution was added carbonyldiimidazole (357 mg) and the mixture was stirred at room temperature for one day and at 50°C for 1 hr. The reaction solvent was evaporated under reduced pressure and the obtained residue was dissolved in ethyl acetate. This solution was washed successively with water, aqueous hydrochloric acid (0.5N), saturated aqueous sodium hydrogen carbonate and water. This solution was dried over anhydrous sodium sulfate and filtrated. The filtrate was evaporated under reduced pressure and the residue was crystallized from ethyl acetate, diethyl ether to give the title compound (80 mg, yield 12%) as white crystals (see Table 23).

Example 3-2

N-(4-oxo-2-thioxo-perhydropyrimidin-3-yl)-5-chloro-1H-indole-2-carboxamide

In the same manner as in Example 3 b) but using thiocarbonyldiimidazole instead of carbonyldiimidazol, the title compound (yield 74%) was obtained (see Table 23).

Example 3-3

N-(2,4-dioxo-1-phenyl-perhydropyrimidin-3-yl)-5-chloro-1H-indole-2-carboxamide

a) 3-anilinopropionic acid

A solution (30 ml) of aniline (5.00 g) in acetonitrile was heated under reflux and β-propiolactone (3.36 ml) was added dropwise. The mixture was heated under reflux for 3 hr and the solvent was evaporated under reduced pressure. The residue was dissolved in aqueous sodium hydroxide solution. This mixture was washed with diethyl ether, adjusted to pH 4-5 with hydrochloric acid and extracted with diethyl ether. The organic layer was washed with water and saturated brine, dried over sodium sulfate, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (chloroform:MeOH=9:1) to give 3-anilinopropionic acid (2.08 g, yield 23%).

b) 5-chloro-1H-indole-2-carboxylic acid 2-(3-anilinopropionyl)hydrazide

To a suspension (10 ml) of 5-chloro-1H-indole-2-carboxylic acid hydrazide obtained in Example 1 a) (419 mg) and compound 3 obtained in Example 3-3 a) (330 mg) in DMF were added 1-hydroxybenzotriazole (368 mg) and EDC (460 mg), and the mixture was stirred at room temperature for 12 hr. Water was added to the reaction solution and the mixture was extracted with ethyl acetate. The organic layer was washed successively with 10% aqueous citric acid solution, saturated aqueous sodium hydrogen carbonate, water and saturated brine and dried over sodium sulfate. This solution was filtered and

concentrated under reduced pressure. The residue was recrystallized from ethyl acetate·n-hexane to give the title compound (468 mg, yield 66%).

c) N-(2,4-dioxo-1-phenyl-perhydropyrimidin-3-yl)-5-chloro-1H-indole-2-carboxamide

To a solution (3 ml) of 5-chloro-1H-indole-2-carboxylic acid 2-(3-anilinopropionyl)hydrazide obtained in Example 3-3 b) (51.0 mg) in THF were added triethylamine (44 mg) and triphosgene (15.6 mg). The mixture was stirred at room temperature for 4 hr and water was added. This mixture was extracted with ethyl acetate. The organic layer was washed with 10% aqueous citric acid solution, saturated aqueous sodium hydrogen carbonate and saturated brine and dried over sodium sulfate. This was filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (n-hexane:ethyl acetate=1:2) to give the title compound (34 mg, yield 62%) (see Table 23).

Example 3-4

N-(4-oxo-1-phenyl-perhydropyrimidin-3-yl)-5-chloro-1H-indole-2-carboxamide

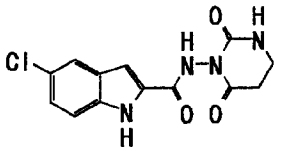
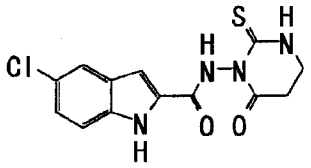
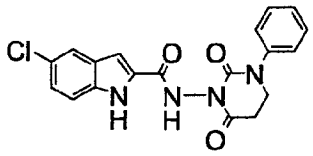
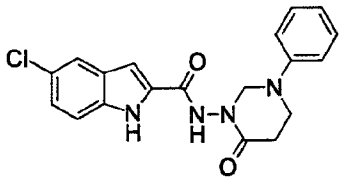
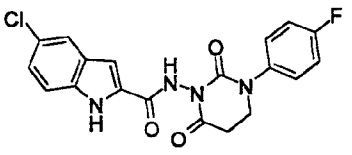
To a suspension of 5-chloro-1H-indole-2-carboxylic acid 2-(3-anilinopropionyl)hydrazide obtained in Example 3-3 b) (100 mg) in ethanol (5 ml) was added paraformaldehyde (68 mg). The mixture was stirred at room temperature for 7 days and water was added. The mixture was extracted with ethyl acetate and the organic layer was washed with saturated brine and dried over sodium sulfate. This solution was filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (chloroform:MeOH=20:1) to give the title compound (48 mg) (see Table 23).

Examples 3-5 and 2-15

In the same manner as in Examples 3 to 3-4, the compounds of Examples 3-5 to 3-15 were obtained. The obtained compounds

are shown in Tables 23-24.

Table-23

Ex.	Structural formula	^{1}H-NMR(δ,300MHz,DMSO-d6)
3		2.80(2H,t,J=6.7Hz), 3.30-3.39(2H,m), 7.20-7.24(2H,m), 7.47(1H,d,J=8.8Hz), 7.77(1H,m), 8.10(1H,brs), 10.75(1H,brs), 11.92(1H,s).
3-2		2.91(2H,t,J=6.9Hz), 3.45(2H,m), 7.234(2H,dd,J=8.8Hz,1.9Hz)), 7.28(1H,s), 7.46(1H,d,J=8.8Hz), 7.78(1H,d,J=1/9Hz), 10.14(1H,s), 11.06(1H,s), 11.92(1H,s).
3-3		—
3-4		—
3-5		3.07(2H,m), 3.90(2H,m), 7.22-7.31(4H,m), 7.42-7.49(3H,m), 7.78(1H,d,J=1.8Hz), 10.92(1H,s), 11.92(1H,s).

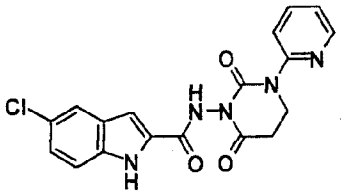
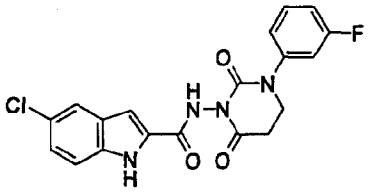
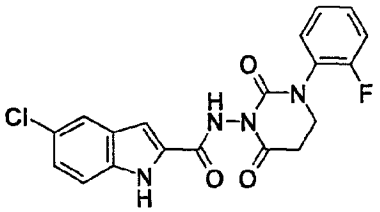
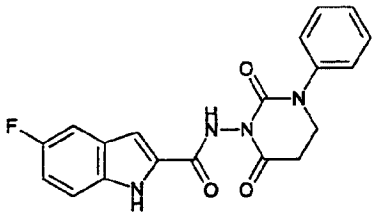
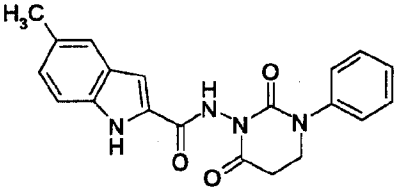
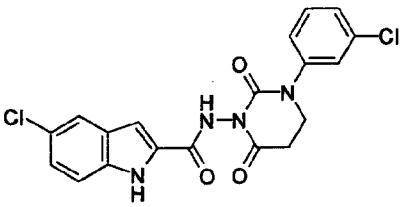
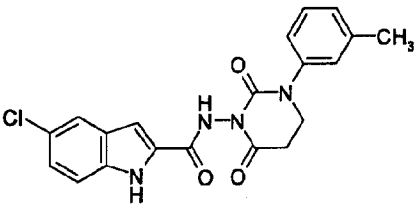
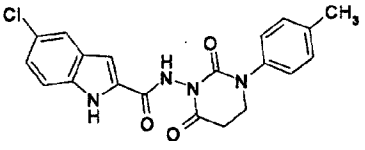
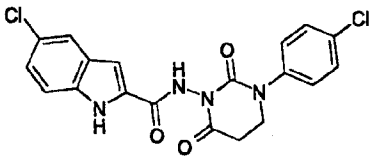
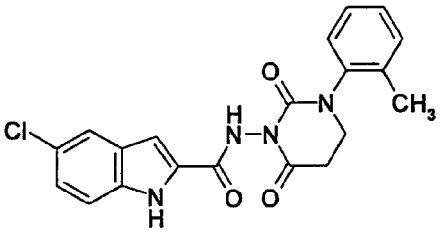
3-6		3.05(2H,m), 4.19(2H,m), 7.22-7.30(3H,m), 7.48(1H,d,J=9.0Hz), 7.73(1H,d,J=8.4Hz), 7.79(1H,d,J=1.8Hz), 7.87(1H,m)8.48(1H,m), 10.99(1H,s), 11.95(1H,s).
3-7		3.07(2H,m), 3.95(2H,m), 7.14(1H,m), 7.22-7.33(4H,m), 7.44-7.52(2H,m), 7.77(1H,s), 10.94(1H,s), 11.93(1H,s).
3-8		3.09(2H,m), 3.86(2H,m), 7.21-7.56(7H,m), 7.77(1H,d,J=2.1Hz), 10.96(1H,s), 11.93(1H,brs).

Table-24

Ex.	Structural formula	^{1}H-NMR(δ,300MHz,DMSO-d6)
3-9		3.07(2H,m), 3.92(2H,m)7.10(1H,m), 7.27-7.31(2H,m), 7.38-7.48(6H,m), 10.87(1H,s)11.82(1H,s).
3-10		2.38(3H,s), 3.06(2H,m), 3.92(2H,m), 7.06(1H,d,J=9.8Hz), 7.19(1H,d,J=1.5Hz), 7.26-7.47(7H,m), 10.77(1H,s), 11.58(1H,s).
3-11		3.08(2H,m), 3.95(2H,m), 7.22-7.28(2H,m), 7.35-7.40(2H,m), 7.45-7.53(3H,m), 7.78(1H,d,J=1.8Hz), 10.94(1H,s), 11.93(1H,s).
3-12		2.33(3H,s), 3.06(2H,m), 3.90(2H,m), 7.10(1H,d,J=7.5Hz), 7.17-7.35(5H,m), 7.48(1H,d,J=8.7Hz), 7.78(1H,d,J=1.8Hz), 10.91(1H,s), 11.92(1H,s).
3-13		2.32(3H,s), 3.05(2H,m), 3.88(2H,m), 7.21-7.29(6H,m), 7.47(1H,d,J=8.7Hz), 7.77(1H,s), 10.90(1H,s), 11.91(1H,s).

3-14		3.07(2H,m), 3.92(2H,m), 7.22-7.28(2H,m), 7.42-7.52(5H,m), 7.78(1H,d,J=1.8Hz), 10.93(1H,s), 11.92(1H,s).
3-15		2.24(3H,s), 3.09(2H,m), 3.70(1H,m), 3.86(1H,m), 7.21-7.31(6H,m), 7.44-7.48(1H,m), 7.77(1H,d,J=1.8Hz), 10.93(1H,m), 11.91(0.5H,s), 11.97(0.5H,s).

Example 4

N-(2,4-dioxo-5-phenylimidazolidin-3-yl)-5-chloro-1H-indole-2-carboxamide

a) tert-butyl 2-[2-(5-chloro-1H-indole-2-carbonyl)hydrazino]-2-oxo-1-phenyl-ethyl}carbamate

To a suspension (10 ml) of 5-chloro-1H-indole-2-carboxylic acid hydrazide obtained in Example 1 a) (420 mg) and 2-(tert-butoxycarbonylamino)-2-phenylacetic acid (503 mg) in DMF were added 1-hydroxybenzotriazole monohydrate (368 mg) and EDC (460 mg). This reaction mixture was stirred at room temperature for 14 hr and water was added to the reaction solution. The reaction mixture was extracted with ethyl acetate. The organic layer was washed successively with 10% aqueous citric acid solution, saturated aqueous sodium hydrogen carbonate, water and saturated brine, and dried over sodium sulfate. This solution was filtered and concentrated under reduced pressure and the residue was recrystallized from ethyl acetate·n-hexane to give the title compound (790 mg, yield 89%).

b) 5-chloro-1H-indole-2-carboxylic acid 2-((a-aminobenzyl)carbonyl)hydrazide

To a suspension (5 ml) of tert-butyl 2-[2-(5-chloro-1H-

indole-2-carbonyl)hydrazino]-2-oxo-1-phenyl-ethyl}carbamate obtained in Example 4 a) (500 mg) in dichloromethane was added trifluoroacetic acid (5 ml) at room temperature. This reaction mixture was stirred at room temperature for 5 hr and alkalized with aqueous sodium hydrogen carbonate. This mixture was extracted with ethyl acetate and the organic layer was washed with water and saturated brine, and dried over sodium sulfate. This solution was filtered and concentrated under reduced pressure. The residue was recrystallized from ethyl acetate·n-hexane to give the title compound (366 mg, yield 94%).

^{1}H-NMR(s)ppm(300MHz,DMSO-d_6)

4.54(1H,s),7.19-

7.37(5H,m),7.44(1H,d,J=8.7Hz),7.54(2H,d,J=7.5Hz),7.71(1H,d,J=1.8Hz),11.91(1H,s).

c) N-(2,4-dioxo-5-phenylimidazolidin-3-yl)-5-chloro-1H-indole-2-carboxamide

To a solution (3 ml) of 5-chloro-1H-indole-2-carboxylic acid 2-((α-aminobenzyl)carbonyl)hydrazide obtained in Example 4 b) (80.0 mg) in THF was added carbonyldiimidazole (45.8 mg) at room temperature. The mixture was stirred at room temperature for 16 hr and 10% aqueous citric acid solution was added. This mixture was extracted with ethyl acetate. The organic layer was washed with water and saturated brine and dried over sodium sulfate. This was filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane:ethyl acetate=1:2) to give the title compound (75 mg, yield 87%) (see Table 25).

Example 4-2

N-(2,4-dioxo-1-phenylimidazolidin-3-yl)-5-chloro-1H-indole-2-carboxamide

a) 5-chloro-1H-indole-2-carboxylic acid 2-(anilinoacetyl)hydrazide

To a suspension (5 ml) of 5-chloro-1H-indole-2-carboxylic

acid hydrazide obtained in Example 1 a) (210 mg) and anilinoacetic acid (151 mg) in DMF were added 1-hydroxybenzotriazole (184 g) and EDC (230 mg). The mixture was stirred at room temperature for 13 hr and water was added to the reaction solution. This mixture was extracted with ethyl acetate. The organic layer was washed successively with 10% aqueous citric acid solution, saturated aqueous sodium hydrogen carbonate, water and saturated brine and dried over sodium sulfate. This solution was filtered and concentrated under reduced pressure. The residue was recrystallized from ethyl acetate-n-hexane to give the title compound (321 mg, yield 94%).

b) N-(2,4-dioxo-1-phenylimidazolidin-3-yl)-5-chloro-1H-indole-2-carboxamide

To a solution (10 ml) of 5-chloro-1H-indole-2-carboxylic acid 2-(anilinoacetyl)hydrazide obtained in Example 4-2 a) (203 mg) in THF was added carbonyldiimidazole (140 mg). The mixture was stirred at 60°C for 13 hr, allowed to cool and 10% aqueous citric acid solution was added. The mixture was extracted with ethyl acetate ester. The organic layer was washed with saturated aqueous sodium hydrogen carbonate and saturated brine and dried over sodium sulfate. This was filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane:ethyl acetate=2:1) to give the title compound (21 mg, yield 10%) (see Table 25).

Example 4-3

N-(4-oxo-1-phenyl-2-thioxoimidazolidin-3-yl)-5-chloro-1H-indole-2-carboxamide

In the same manner as in Example 4-2 b) but using thiocarbonyldiimidazole instead of carbonyldiimidazole, the title compound was obtained (see Table 25).

Example 4-4

N-(1-oxo-4-phenylimidazolidin-2-yl)-5-chloro-1H-indole-2-carboxamide

To a suspension of 5-chloro-1H-indole-2-carboxylic acid 2-(anilinoacetyl)hydrazide obtained in Example 4-2 a) (103 mg) in ethanol (3 ml) was added paraformaldehyde (36 mg). The mixture was stirred at room temperature for 5 days, and water was added. This mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over sodium sulfate. This solution was filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane:ethyl acetate=2:1) to give the title compound (73 mg, yield 69%) (see Table 25).

Example 4-5

N-(2-oxo-1-phenylimidazolidin-3-yl)-5-chloro-1H-indole-2-carboxamide

a) 1-(5-chloro-1H-indole-2-carbonyl)-4-phenylsemicarbazide

To a suspension of 5-chloro-1H-indole-2-carboxylic acid hydrazide obtained in Example 1 a) (800 mg) in THF (10 ml) was added phenylisocyanate (477 mg). The mixture was stirred at room temperature for 2 hr and diethyl ether was added. The precipitated solid was collected by filtration and dried in vacuo to give the title compound (1.24 g, yield 99%).

b) N-(2-oxo-1-phenylimidazolidin-3-yl)-5-chloro-1H-indole-2-carboxamide

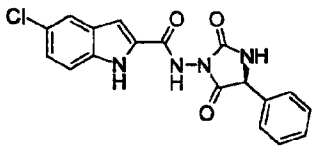
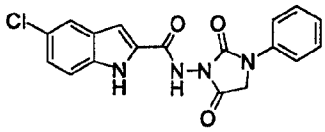
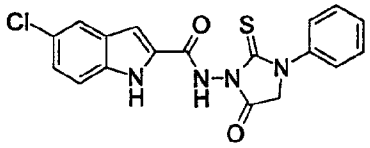
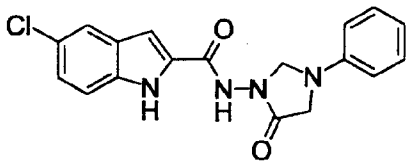
To a solution of 1-(5-chloro-1H-indole-2-carbonyl)-4-phenylsemicarbazide obtained in Example 4-5 a) (100 mg) in DMF (5 ml) were added 1,2-dibromoethane (63 mg) and potassium carbonate (92 mg) and the mixture was stirred at 60°C for 18 hr. The mixture was allowed to cool and 10% aqueous citric acid solution was added. The mixture was extracted with ethyl acetate and the organic layer was washed with saturated aqueous sodium hydrogen carbonate, water and saturated brine,

and dried over sodium sulfate. This solution was filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane:ethyl acetate=2:1) to give the title compound (45 mg, yield 42%) (see Table 25).

Examples 4-6 to 4-20

In the same manner as in Examples 4 to 4-5, the compounds of Examples 4-6 to 4-20 were obtained. The obtained compounds are shown in Tables 25-27.

Table-25

Ex.	Structural formula	^{1}H-NMR(δ,300MHz,DMSO-d6)
4		5.48(0.6H,s), 5.59(0.4H,s), 7.24-7.32(2H,m), 7.41-7.54(6H,m), 7.81(1H,s), 9.05(0.6H,s), 9.14(0.4H,s), 11.19(0.4H,s), 11.30(0.6H,s), 12.11(1H,s).
4-2		4.79(1H,d,J=18Hz), 4.90(1H,d,J=18Hz), 7.18-7.28(2H,m), 7.35(1H,s), 7.43-7.50(3H,m), 7.68(2H,m), 7.82(1H,s), 11.38(1H,s), 12.06(1H,s).
4-3		5.04(1H,d,J=19Hz), 5.14(1H,d,J=19Hz), 7.26(1H,dd,J=1.8, 8.7Hz), 7.38(2H,m), 7.47-7.54(3H,m), 7.77-7.83(3H,m), 11.49(1H,s), 12.04(1H,brs).
4-4		4.06(2H,s), 4.89(2H,s), 6.67(2H,d,J=8.1Hz), 6.80(1H,t,J=7.3Hz), 7.23-7.30(4H,m), 7.48(1H,d,J=8.8Hz), 7.80(1H,d,J=1.8Hz), 11.10(1H,s), 12.06(1H,s).

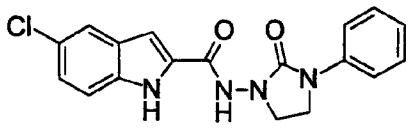
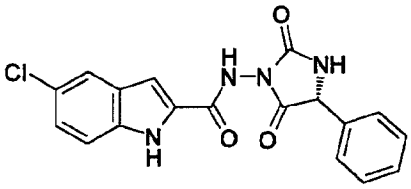
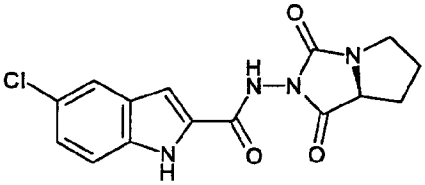
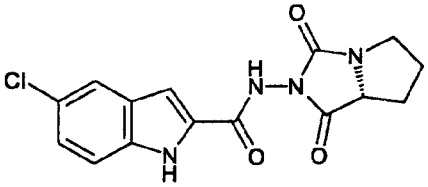
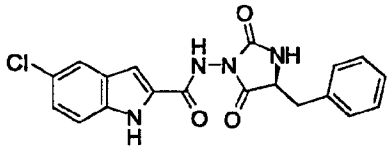
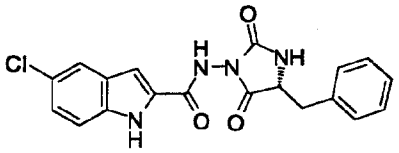
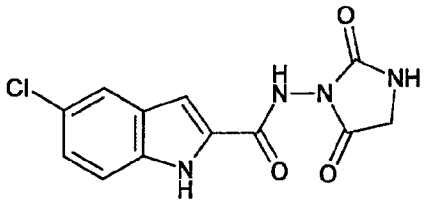
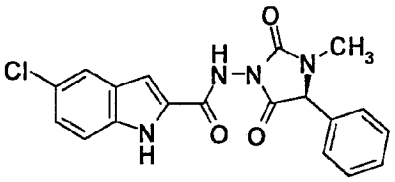
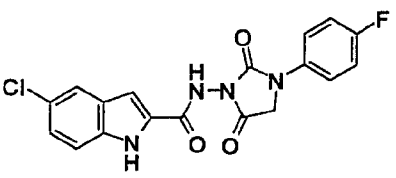
4-5		3.95(2H,m), 4.52(2H,m), 6.85(1H,s), 7.07(1H,t,J=7.5Hz), 7.21(1H,dd,J=2.1,8.7Hz), 7.36(2H,dd,J=7.5, 7.5Hz), 7.49(1H,d,J=8.7Hz), 7.64(3H,m), 9.23(1H,s), 11.84(1H,s).
4-6		5.47(0.6H,s), 5.59(0.4H,s), 7.24-7.32(2H,m), 7.41-7.54(6H,m), 7.80(1H,s), 9.04(0.6H,s), 9.12(0.4H,s), 11.17(0.4H,s), 11.29(0.6H,s), 12.09(1H,s).
4-7		1.68(1H,m), 2.08(2H,m), 2.27(1H,m), 3.32(1H,m), 3.58(1H,m), 4.42(1H,m), 7.26(1H,dd,J=2.1, 8.7Hz), 7.27(1H,s), 7.47(1H,d,J=8.7Hz), 7.80(1H,d,J=2.1Hz), 11.24(1H,s), 12.00(0.6H,brs), 12.07(0.4H,brs).
4-8		1.68(1H,m), 2.07(2H,m), 2.28(1H,m), 3.32(1H,m), 3.59(1H,m), 4.43(1H,m), 7.24-7.28(2H,m), 7.47(1H,d,J=8.8Hz), 7.80(1H,s), 11.24(1H,s), 12.01(0.6H,brs), 12.07(0.4H,brs).

Table-26

Ex.	Structural formula	^{1}H-NMR(δ,300MHz,DMSO-d6)
4-9		2.90-3.17(2H,m), 4.62-4.72(1H,m), 7.23-7.35(7H,m), 7.46(1H,m), 7.77(1H,m), 8.57(0.3H,s), 8.64(0.7H,s), 11.04(0.7H,s), 11.08(0.3H,s), 11.99(0.7H,s), 12.03(0.3H,s).
4-10		2.90-3.19(2H,m), 4.62-4.72(1H,m), 7.23-7.35(7H,m), 7.46(1H,m), 7.77(1H,m), 8.57(0.3H,s), 8.64(0.7H,s), 11.04(0.7H,s), 11.08(0.3H,s), 11.99(0.7H,s), 12.03(0.3H,s).
4-11		4.18(2H,s), 7.25(1H,dd,J=2.1, 8.9Hz), 7.30(1H,s), 7.47(1H,d,J=8.9Hz), 7.80(1H,s), 8.40(1H,s), 11.09(1H,s), 12.03(1H,brs).
4-12		2.73(3H,s), 5.65(1H,s), 7.20(1H,dd,J=2.1, 8.7Hz), 7.34-7.51(7H,m), 7.69(1H,m), 11.13(1H,s), 11.89(1H,brs).
4-13		4.79(1H,d,J=17Hz), 4.90(1H,d,J=17Hz), 7.25-7.36(4H,m), 7.49(1H,d,J=8.8Hz), 7.68-7.72(2H,m), 7.82(1H,s), 11.38(1H,s), 12.07(1H,s).

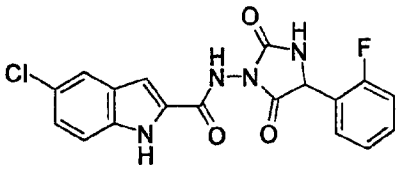
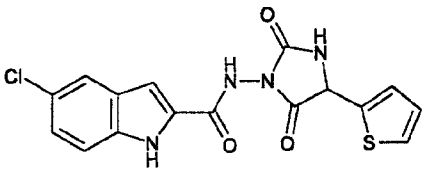
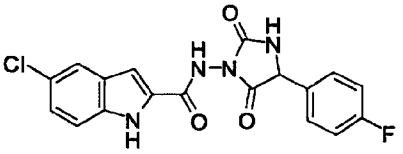
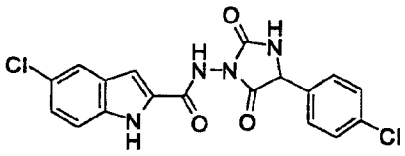
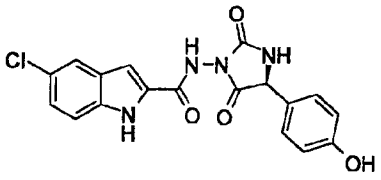
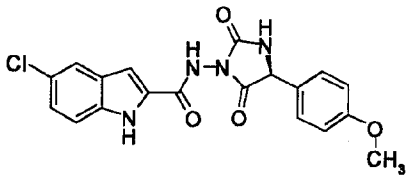
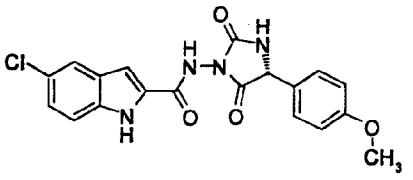
4-14		5.73(1H,m), 7.24-7.35(4H,m), 7.45-7.57(3H,m), 7.81(1H,d,J=1.8Hz), 9.01(1H,m), 11.31(1H,s), 12.08(1H,m).
4-15		5.83(0.5H,s), 5.95(0.5H,s), 7.10(1H,m), 7.24-7.31(3H,m), 7.47(1H,m), 7.61(1H,m), 7.81(1H,d,J=1.8Hz), 9.22(0.5H,s), 9.34(0.5H,s), 11.26(1H,s), 12.08(1H,s).
4-16		5.51(0.6H,s), 5.63(0.4H,s), 7.24-7.34(4H,m), 7.45-7.56(3H,m), 7.80(1H,s), 9.05(0.6H,s), 9.14(0.4H,s), 11.30(1H,brs), 12.10(1H,s).

Table-27

Ex.	Structural formula	^{1}H-NMR(δ,300MHz,DMSO-d6)
4-17		5.53(0.6H,s), 5.66(0.4H,s), 7.24-7.32(2H,m), 7.44-7.57(5H,m), 7.80(1H,s), 9.08(0.6H,s), 9.16(0.4H,s), 11.18(0.4H,brs), 11.32(0.6H,s), 12.09(1H,s).
4-18		5.32(0.6H,s), 5.41(0.4H,s), 6.81(2H,m), 7.18-7.32(4H,m), 7.46(1H,m), 7.80(1H,s), 8.90(0.6H,s), 8.99(0.4H,s), 9.60(1H,s), 11.15(0.4H,s), 11.24(0.6H,s), 12.09(1H,m).
4-19		3.78(3H,s), 5.40(0.6H,s), 5.51(0.4H,s), 6.99-7.04(2H,m), 7.24-7.34(3H,m), 7.42-7.47(2H,m), 7.81(1H,s), 8.98(0.6H,s), 9.07(0.4H,s), 11.17(0.4H,s), 11.28(0.6H,s), 12.11(1H,m).
4-20		3.78(3H,s), 5.41(0.6H,s), 5.51(0.4H,s), 6.99-7.04(2H,m), 7.25-7.34(3H,m), 7.42-7.49(2H,m), 7.81(1H,s), 8.98(0.6H,s), 9.07(0.4H,s), 11.18(0.4H,s), 11.29(0.6H,s), 12.09(0.4H,s), 12.12(0.6H,s).

Example 5

1-(5-chloro-1H-indole-2-carbonyl)-4-phenylsemicarbazide

5-Chloro-1H-indole-2-carboxylic acid hydrazide obtained in Example 1 a) (105 mg) and phenylisocyanate (54 μl) were reacted in dioxane (1 ml) for 1 hr. THF (5 ml) was added to the reaction mixture and the mixture was heated at 60°C for 1 hr. This reaction solution was concentrated and stood to allow precipitation of crystals. The crystals were collected by filtration and dried in vacuo to give the title compound (144 mg, yield 88%) (see Table 28).

Example 5-2

5-chloro-1H-indole-2-carboxylic acid 2-(phenylthio)carbonylhydrazide

In the same manner as in Example 5-1 but using phenyl isothiocyanate instead of phenylisocyanate, the title compound was obtained (yield 23%) (see Table 28).

Example 5-3

5-chloro-1H-indole-2-carboxylic acid 2-phenylacetylhydrazide

5-chloro-1H-indole-2-carboxylic acid hydrazide obtained in Example 1 a) (91.1 mg) was suspended in THF, and triethylamine (0.05 ml) and phenylacetylchloride (0.065 ml) were successively added. The mixture was stirred at room temperature for 1 hr and 30 min. Water (2 ml) and sodium hydrogen carbonate (34 mg) were successively added to the reaction mixture and the mixture was stirred for 1 hr. The precipitated solid was collected by filtration to give the title compound (112 mg, yield 79%) as a colorless solid(see Table 28).

Example 5-4

5-chloro-1H-indole-2-carboxylic acid 2-(benzoylformyl)hydrazide

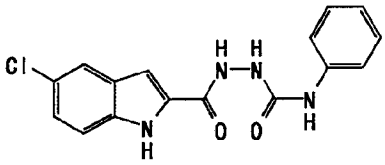
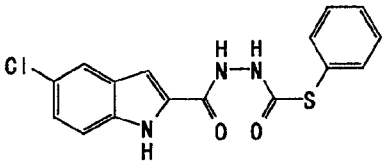
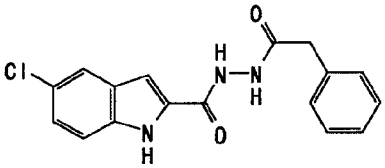
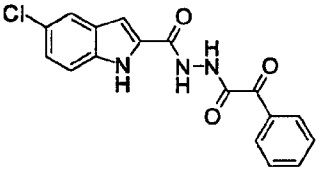
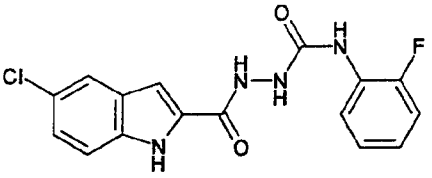
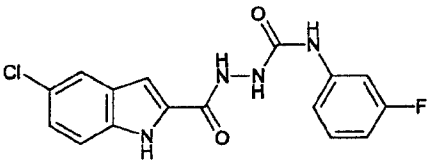
To a suspension (5 ml) of 5-chloro-1H-indole-2-carboxylic acid hydrazide obtained in Example 1 a) (240 mg) and

benzoylformic acid (150 mg) in DMF were added 1-hydroxybenzotriazole (184 mg) and EDC (230 mg). The mixture was stirred at room temperature for 14 hr and water was added to the reaction solution. This mixture was extracted with ethyl acetate. The organic layer was washed successively with 10% aqueous citric acid solution, saturated aqueous sodium hydrogen carbonate, water and saturated brine, and dried over sodium sulfate. This solution was filtered and concentrated under reduced pressure. The residue was washed with diethyl ether to give the title compound (106 mg) (see Table 28).

Examples 5-5 to 5-19

In the same manner as in Examples 5 to 5-4, the compounds of Examples 5-5 to 5-19 were obtained. The obtained compounds are shown in Tables 28-30.

Table-28

Ex.	Structural formula	^{1}H-NMR(δ,300MHz,DMSO-d6)
5		6.96(1H,t,J=7.3Hz), 7.19-7.29(4H,m,), 7.44-7.50(3H,m), 8.26(1H,s), 8.90(1H,s), 10.39(1H,s), 11.93(1H,s).
5-2		7.13-7.23(3H,m), 7.32(2H,d,J=7.8Hz), 7.46(3H,m), 7.75(1H,s), 9.76(1H,s), 9.89(1H,s), 10.62(1H,s), 11.94(1H,s).
5-3		3.56(2H,s), 7.197.38(7H,m,), 7.44(1H,d,J=8.8Hz), 7.72(1H,d,J=1.8Hz), 10.23(1H,s), 10.50(1H,s), 11.92(1H,s).
5-4		7.23(2H,m), 7.47(1H,d,J=8.4Hz), 7.65(2H,m), 7.79(2H,m), 8.16(2H,m), 10.80(1H,s), 11.00(1H,s), 12.06(1H,s).
5-5		7.03(1H,m), 7.13(1H,m), 7.20-7.27(3H,m) 7.46(1H,d,J=8.7Hz), 7.75(1H,d,J=1.8Hz) 8.00(1H,m), 8.56(1H,s), 8.67(1H,s) 10.47(1H,s), 11.92(1H,s).
5-6		6.77(1H,m), 7.20-7.33(4H,m), 7.44-7.51(2H,m), 7.75(1H,d,J=1.8Hz), 8.40(1H,s), 9.13(1H,s), 10.39(1H,s), 11.92(1H,s).

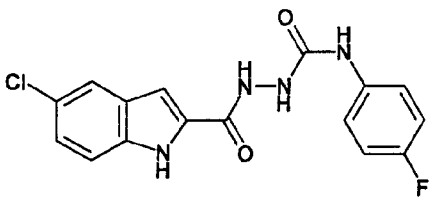
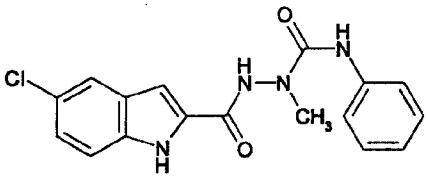
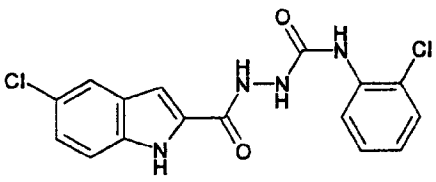
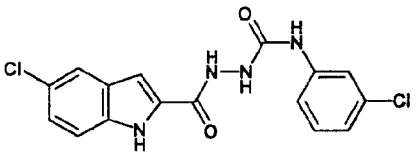
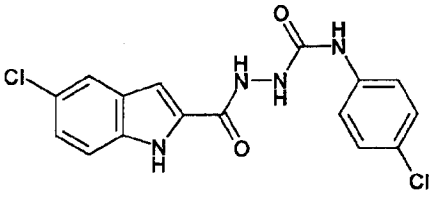
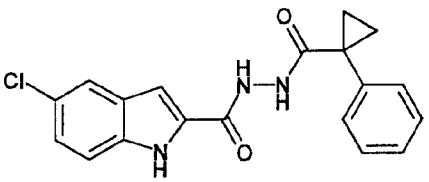
5-7		7.10(2H,m), 7.19-7.23(2H,m), 7.44-7.52(3H,m), 7.74(1H,d,J=2.4Hz), 8.29(1H,s), 8.94(1H,s), 10.37(1H,s), 11.91(1H,s).
5-8		3.12(3H,s), 6.96(1H,d,J=7.3Hz), 7.21-7.26(4H,m), 7.45-7.52(3H,m), 7.77(1H,d,J=1.8Hz), 8.86(1H,s), 10.66(1H,s), 11.97(1H,s).

Table-29

Ex.	Structural formula	^{1}H-NMR(δ,300MHz,DMSO-d6)
5-9		7.05(1H,ddd,J=1.5,7.8,7.8Hz), 7.20-7.24,(2H,m), 7.30(1H,ddd,J=1.5,7.0,7.0Hz), 7.44-7.48(2H,m), 7.75(1H,d,J=1.8Hz), 8.09(1H,d,J=7.8Hz), 8.36(1H,s), 8.97(1H,s), 10.53(1H,s), 11.95(1H,s).
5-10		7.01(1H,d,J=6.7Hz), 7.20-7.31(3H,m), 7.39-7.47(2H,m), 7.71(1H,d,J=1.9Hz), 7.75(1H,d,J=1.9Hz), 8.43(1H,s), 9.12(1H,s), 10.41(1H,s), 11.94(1H,s).
5-11		7.19-7.23(2H,m), 7.31(2H,d,J=8.6Hz), 7.46(1H,d,J=8.6Hz), 7.53(2H,d,J=8.6Hz), 7.74(1H,d,J=1.8Hz), 8.35(1H,s), 9.05(1H,s), 10.38(1H,s), 11.91(1H,s).
5-12		1.10(2H,m), 1.41(2H,m), 7.15-7.22(2H,m), 7.26-7.45(6H,m), 7.72(1H,d,J=1.9Hz), 9.18(1H,s), 10.36(1H,s), 11.85(1H,s).

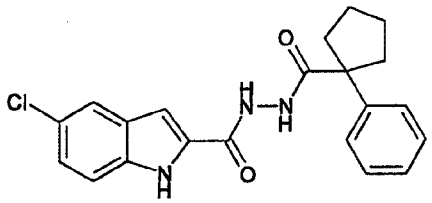
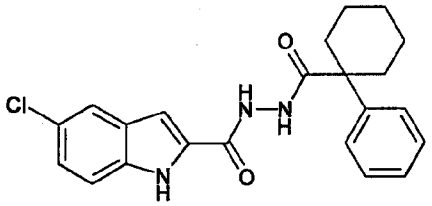
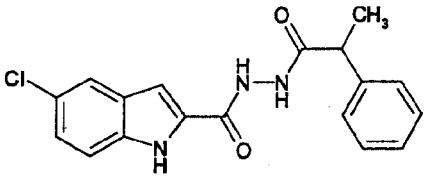
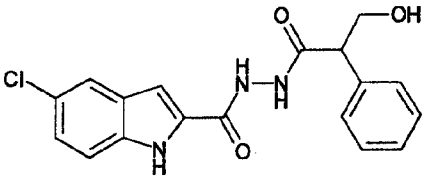
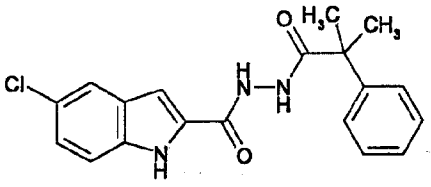
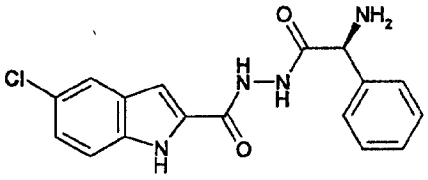
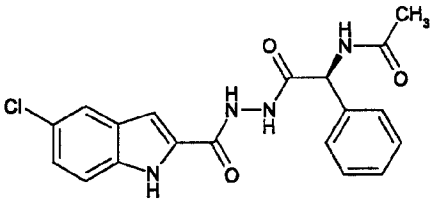
5-13		1.71-1.87(6H,m), 2.68(2H,m), 7.15-7.25(3H,m), 7.30-7.35(2H,m), 7.41-7.47(3H,m), 7.71(1H,s), 9.65(1H,s), 10.30(1H,s), 11.89(1H,s).
5-14		1.28(1H,m), 1.60-1.69(7H,m), 2.51(2H,m), 7.18-7.25(3H,m), 7.34(2H,m), 7.41-7.51(3H,m), 7.72(1H,d,J=1.9Hz), 9.68(1H,s), 10.33(1H,s), 11.94(1H,s).
5-15		1.41(3H,d,J=7.0Hz), 3.77(1H,q,J=7.0Hz), 7.17-7.27(3H,m), 7.33(2H,m), 7.40-7.45(3H,m), 7.72(1H,d,J=2.0Hz), 10.17(1H,s), 10.47(1H,s), 11.90(1H,s).
5-16		3.63(1H,m), 3.77(1H,m), 3.98(1H,m), 4.91(1H,t,J=5.2Hz), 7.18-7.45(8H,m), 7.72(1H,d,J=1.9Hz), 10.21(1H,s), 10.51(1H,s), 11.89(1H,s).

Table-30

Ex.	Structural formula	^{1}H-NMR(δ,300MHz,DMSO-d6)
5-17		1.54(6H,s), 7.19-7.26(3H,m), 7.34(2H,m), 7.42-7.51(3H,m), 7.73(1H,d,J=1.8Hz), 9.60(1H,s), 10.36(1H,s), 11.92(1H,s).
5-18		4.54(1H,s), 7.19-7.37(5H,m), 7.44(1H,d,J=8.7Hz), 7.54(2H,d,J=7.5Hz), 7.71(1H,d,J=1.8Hz), 11.91(1H,s).
5-19		1.93(3H,s), 5.70(1H,d,J=8.4Hz), 7.19-7.22(2H,m), 7.31-7.45(4H,m), 7.55(2H,m), 7.73(1H,s), 8.71(1H,d,J=8.4Hz), 10.52(1H,s), 10.56(1H,s), 11.93(1H,s).

Example 6

5-chloro-1H-indole-2-carboxylic acid 2-(imino-phenyl-methyl)hydrazide hydrochloride

To a suspension (530 ml) of 5-chloro-1H-indole-2-carboxylic acid 2-(imino-phenyl-methyl)hydrazide obtained in Example 1-7 (35.6 g) in MeOH was added dropwise 4N hydrochloric acid/ethyl acetate solution (34.2 ml) under ice-cooling and the mixture was stirred at room temperature for 1 hr. To this reaction solution was added isopropyl ether and the precipitated crystals were collected by filtration and washed with isopropyl ether. This was dried in vacuo to give the title compound (30.3 g, yield 76%) (see Table 31).

Example 6-2

2-amino-4,5-difluorobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide benzenesulfonate

2-Amino-4,5-difluorobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide obtained in Example 1-67 (67.6 mg) and benzenesulfonic acid monohydrate (51.2 mg) were heated at 60°C in THF (1.0 ml) to give a solution. This solution was stood at room temperature for 2 hr to allow precipitation of crystals. The crystals were separated, washed with THF and dried in vacuo to give the title compound (83.3 mg, yield 85%) as pale-yellow needle crystals (see Table 31).

Example 6-3

2-amino-4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide benzenesulfonate

2-Amino-4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide (694.0 mg) obtained in the same manner as in Example 1-97 and benzenesulfonic acid monohydrate (475.0 mg) were heated at 65°C in methanol (70 ml) to give a solution. This solution was concentrated to about 10 ml to allow precipitation of crystals. The crystals were separated, washed with ethanol and dried in vacuo to give the title compound (900.0 mg, 89%) as colorless needle crystals (see Table 31).

Example 6-4

3-(dimethylamino)benzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide methanesulfonate

3-(Dimethylamino)benzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide obtained in Example 1-45 (68.3 mg) and methanesulfonic acid (19 μl) were dissolved in methanol (0.7 ml) at room temperature. Diethyl ether (1.0 ml) was added dropwise to this solution to allow precipitation of needle crystals. The crystals were separated, washed with diethyl ether and dried in vacuo to give the title compound (72.8 mg, 84%) as colorless needle crystals (see Table 31).

Example 6-5

2-amino-4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide hydrochloride

2-Amino-4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide obtained in Example 1-97 (93 mg) was suspended in methanol (7.0 ml). A 4N hydrochloric acid-dioxane solution (0.55 ml) was added to this mixture and the mixture was heated to 60°C to give a solution. Diethyl ether (5 ml) was added dropwise to the obtained solution. The obtained mixture was stood for 1 hr to allow precipitation of white crystals. The precipitated crystals were collected by filtration, washed with methanol and dried in vacuo to give the title compound (670 mg, 87%) as colorless needle crystals (see Table 31).

Example 6-6

2-amino-4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide p-toluenesulfonate

2-Amino-4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide obtained in Example 1-97 (693 mg) and p-toluenesulfonic acid monohydrate (571 mg) were dissolved in DMSO (2.5 ml). The obtained solution was added dropwise to methanol (6 ml) over 3 min with stirring. The precipitated crystals were collected by filtration, washed with methanol and dried in vacuo to give the title compound (897 mg, 86%) as colorless needle crystals (see Table 31).

Example 6-7

2-amino-4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide p-toluenesulfonate

2-Amino-4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide obtained in Example 1-97 (1.73 g) was dissolved in a THF:H_2O (10:1) mixed solvent (10 ml). p-Toluenesulfonic acid monohydrate (1.05 g) was dissolved in THF (1 ml) and the mixture was heated to 60°C. A solution of 2-

amino-4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide in water-containing THF was added dropwise to a solution of p-toluenesulfonic acid in THF at 60°C. After the completion of the dropwise addition, this mixture was stirred at room temperature for 3 hr. The precipitated crystals were collected by filtration, washed with THF and dried in vacuo to give the title compound (1.99 g, 77%) as colorless needle crystals (see Table 31).

Example 6-8

2-amino-4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide p-toluenesulfonate

2-Amino-4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide obtained in Example 1-97 (5.00 g) was dissolved in a mixture (47.5 ml) of THF:methanol:H_2O (70:30:10) at 60°C. To this solution was added dropwise a mixture (4.1 ml) of p-toluenesulfonic acid (4.11 g) in THF:methanol:H_2O (70:30:10) over 5 min with stirring while maintaining at 60°C. After the completion of the dropwise addition, this mixture was stirred at room temperature for 3 hr. The precipitated crystals were treated in the same manner as in Example 1 to give the title compound (6.42 g, 86%) as colorless needle crystals (see Table 31).

Example 6-9

2-amino-4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide p-toluenesulfonate

2-Amino-4-fluorobenzoic acid 2-(5-chloro-1H-indole-2-carbonyl)hydrazide obtained in Example 1-97 (347 mg) and p-toluenesulfonic acid monohydrate (190 mg) were suspended in n-hexane (15 ml). This mixture was stirred at room temperature for one week. The obtained crystals were collected by filtration, washed with n-hexane and dried in vacuo to give the title compound (430mg,83%) as a white powder (see Table 32).

Example 6-10

2-aminobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide p-toluenesulfonate

The compound was produced using a compound obtained in Example 1-62 as a starting material and according to the method of Example 6-8 (see Table 32).

Example 6-11

2-aminobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide benzenesulfonate

The compound was produced using a compound obtained in Example 1-62 as a starting material and according to the method of Example 6-2 (see Table 32).

Example 6-12

2-amino-4-fluorobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide benzenesulfonate

The compound was produced using a compound obtained in Example 1-63 as a starting material and according to the method of Example 6-2 (see Table 32).

Example 6-13

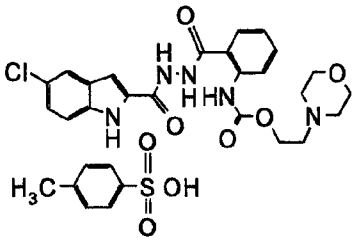
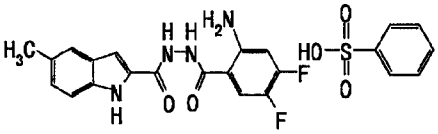
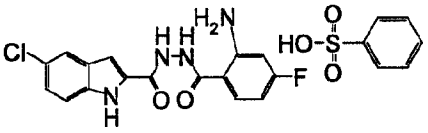
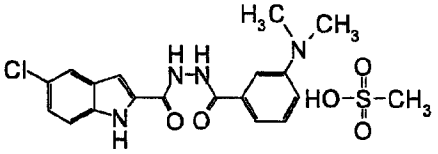
3-aminobenzoic acid 2-(5-methyl-1H-indole-2-carbonyl)hydrazide p-toluenesulfonate

The compound was produced using a compound obtained in Example 1-142 as a starting material and according to the method of Example 6-8 (see Table 32).

Examples 6-14 to 6-35

In the same manner as in Examples 6 to 6-13, the compounds of Examples 6-14 to 6-35 were obtained. The obtained compounds are shown in Tables 31-35.

Table-31

Ex.	Structural formula	^{1}H-NMR(δ,300MHz,DMSO-d6)
6-1		2.28(3H,s), 3.14(2H,m), 3.48(4H,m), 3.64(2H,m), 3.93(2H,m), 4.45(2H,m), 7.10(2H,m), 7.19-7.27(3H,m), 7.48(3H,m), 7.63(1H,m), 7.77(1H,s), 7.89(1H,d,J=6.9Hz), 8.28(1H,d,J=8.4Hz), 9.76(1H,brs), 10.67(1H,s), 10.70(1H,s), 10.83(1H,s), 11.95(1H,s).
6-2		2.38(3H,s), 6.73(1H,dd,J=13.3,7.3Hz), 7.05(1H,d,J=7.1Hz) ,7.17(1H,s) , 7.30-7.36(4H,m), 7.42(1H,s), 7,59-7,62(2H,m), 7.71(1H,dd,J=12.0,9.0Hz), 10.23(1H,m), 10.37(1H,m), 11.57(1H,s).
6-3		6.40(1H,m), 6.52(1H,dd,J=11.9,2.6Hz), 7.20-7.33(5H,m), 7.46(1H,d,J=8.8Hz), 7.58-7.61(2H,m), 7.69-7,76(2H,m), 10.23(1H,s), 10.49(1H,s), 11.94(1H,s).
6-4		2.38(3H,s), 3.02(6H,s), 7.13(1H,brs), 7.20-7.26(2H.m), 7.38-7.48(4H,m), 7.70(1H,d,J=9.6,6.6Hz), 7.76(1H,s), 10.48(1H,s), 10.59(1H,s), 11.92(1H,s).

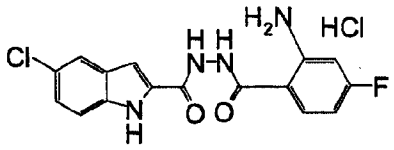
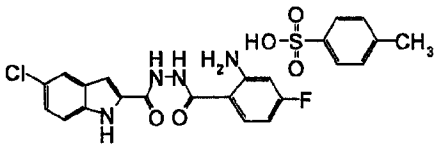
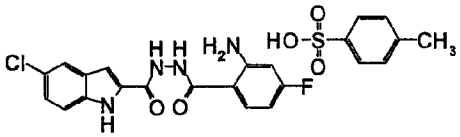
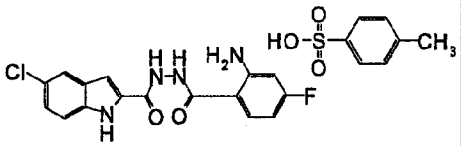
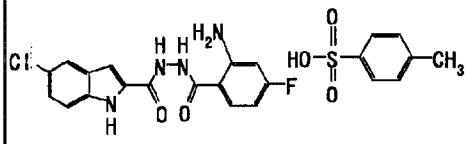
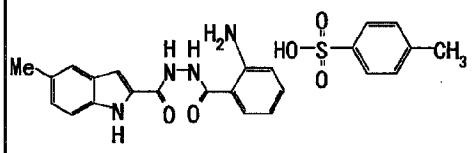
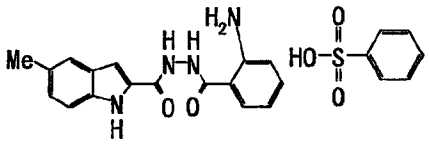
6-5		6.40(1H,dt,J=8.7,2.4Hz), 6.53,(1H,dd,J=11.7,2.7Hz), 7.20-7.25,(2H,m), 7.46(1H,d,J=12.0Hz), 7.71,(1H,dd,J=8.7,6.9Hz), 7.75,(1H,d,J=2.1Hz), 10.25(1H,s), 10.51(1H,s), 11.96(1H,s).
6-6		2.29(3H,s), 6.39(1H,dt,J=8.6,3.6Hz), 6.53(1H,dd,J=11.8,2.9Hz), 7.12,(2H,d,J=8.1Hz), 7.20-7.25(2H,m), 7.45-7.50(3H,m), 7.70(1H,t,J=2.4Hz), 7.75(1H,m), 10.22(1H,s), 10.47(1H,m), 11.91(1H,s).
6-7		2.29(3H,s), 6.39(1H,dt,J=8.6,3.6Hz), 6.53(1H,dd,J=11.8,2.9Hz), 7.12,(2H,d,J=8.1Hz), 7.20-7.25(2H,m), 7.45-7.50(3H,m), 7.70(1H,t,J=2.4Hz), 7.75(1H,m), 10.22(1H,s), 10.47(1H,m), 11.91(1H,s).
6-8		2.29(3H,s), 6.39(1H,dt,J=8.6,3.6Hz), 6.53(1H,dd,J=11.8,2.9Hz), 7.12,(2H,d,J=8.1Hz), 7.20-7.25(2H,m), 7.45-7.50(3H,m), 7.70(1H,t,J=2.4Hz), 7.75(1H,m), 10.22(1H,s), 10.47(1H,m), 11.91(1H,s).

Table-32

Ex.	Structural formula	^{1}H-NMR(δ,300MHz,DMSO-d6)
6-9		2.29(3H,s), 6.39(1H,dt,J=8.6,3.6Hz), 6.53(1H,dd,J=11.8,2.9Hz), 7.12,(2H,d,J=8.1Hz), 7.20-7.25(2H,m), 7.45-7.50(3H,m), 7.70(1H,t,J=2.4Hz), 7.75(1H,m), 10.22(1H,s), 10.47(1H,m), 11.91(1H,s).
6-10		2.28(3H,s), 2.37(3H,s), 5.14(2H,m), 6.72(1H,m), 6.86(1H.m), 7.05(1H,d,J=8.4Hz), 7.12(2H,d,J=8.0Hz), 7.19(1H,s), 7.33(2H,m), 7.43(1H,s), 7.48(2H,d,J=7.4Hz), 7.67(1H,m), 10.24(1H,m), 10.37(1H,s), 11.56(1H,s).
6-11		2.38(3H,s), 4.56(2H,m), 6.69(1H,m), 6.83,(1H,m), 7.05(1H,d,J=8.4Hz), 7.18(1H,s), 7.30-7.43(5H.m), 7.58-7.62(2H,m), 7.66,(1H,m), 7.76(1H,d,J=1.8Hz), 10.24(1H,m), 10.36(1H,s), 11.58(1H,s).

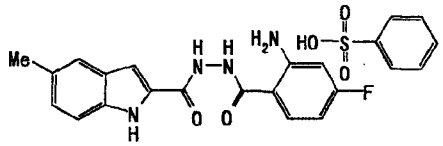
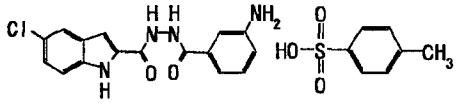
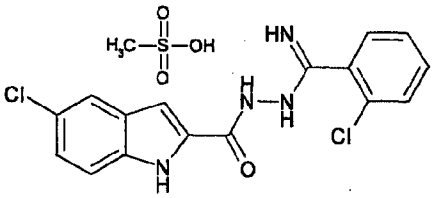
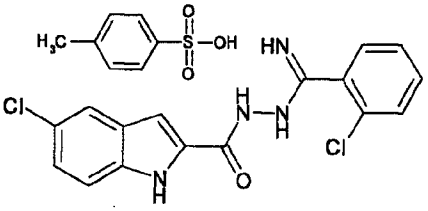
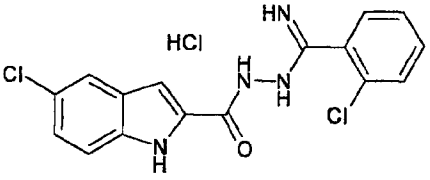
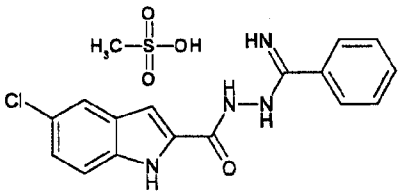
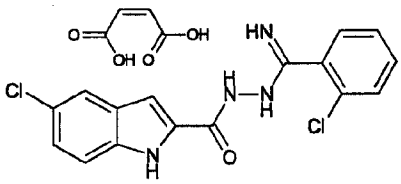
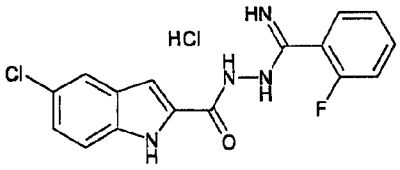
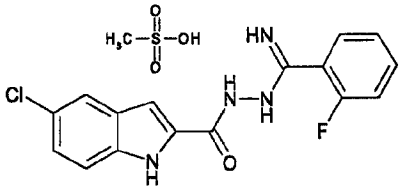
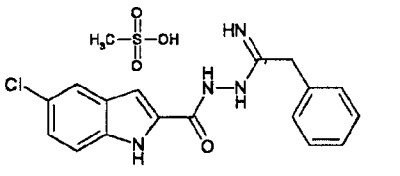
6-12		2.38(3H,s), 5.89(2H,m), 6.39(1H,m), 6.52(1H,dd,J=11.2,2.6Hz), 7.04(1H,d,J=8.4Hz), 7.17(1H,s), 7.30-7.35(4H,m), 7.42(1H,s), 7.59-7.62(2H,m), 7.69(1H,m), 10.18(1H,brs), 10.33(1H,s), 11.57(1H,s).
6-13		2.29(3H,s), 7.11(2H,d,J=7.9Hz), 7.21-7.32(3H,m) ,7.46-7.52(4H,m), 7.63-7.69(2H,m), 7.76(1H,s), 10.58,(1H,s), 10.62(1H,s), 11.93(1H,s).
6-14		2.30(3H,s), 7.27(1H,dd,J=2.1, 8.8Hz), 7.31(1H,d,J=1.5Hz), 7.50(1H,d,J=8.8Hz), 7.64-7.78(4H,m), 7.83(1H,d,J=1.9Hz), 10.12(2H,brs), 11.48(1H,brs), 12.10(2H,brs).
6-15		2.28(3H,s), 7.11(2H,d,J=7.9Hz), 7.27(1H,dd,J=2.1, 8.8Hz), 7.31(1H,d,J=1.5Hz), 7.46-7.51(3H,m), 7.67-7.77(4H,m), 7.82(1H,d,J=1.9Hz), 10.12(2H,brs), 11.48(1H,brs), 12.10(2H,brs).
6-16		7.26(1H,dd,J=2.1, 8.8Hz), 7.36(1H,d,J=1.5Hz), 7.50(1H,d,J=8.8Hz), 7.65-7.77(4H,m), 7.81(1H,d,J=1.9Hz), 10.12(2H,brs), 11.64(1H,brs), 12.16(2H,brs).

Table-33

Ex.	Structural formula	^{1}H-NMR(δ,300MHz,DMSO-d6)
6-17		2.30(3H,s), 7.27(1H,dd,J=2.1, 8.7Hz), 7.32(1H,s), 7.50(1H,d,J=8.7Hz), 7.68-7.73(2H,m), 7.80-7.88(4H,m), 9.84(2H,brs), 11.38(1H,s), 11.84(1H,brs), 12.09(1H,s).
6-18		6.08(2H,s), 7.25(1H,d,J=8.8Hz), 7.29(1H,s), 7.48(1H,d,J=8.8Hz), 7.58-7.72(4H,m), 7.80(1H,s), 9.38(1H,brs), 11.16(1H,brs), 12.02(1H,s).
6-19		7.26(1H,dd,J=1.8, 8.7Hz), 7.38(1H,s), 7.48-7.59(3H,m), 7.74-7.85(3H,m), 10.11(2H,brs), 11.70(1H,brs), 12.16(2H,brs).
6-20		2.30(3H,s), 7.27(1H,dd,J=1.8, 8.7Hz), 7.30(1H,s), 7.49-7.60(3H,m), 7.74-7.82(3H,m), 10.06(2H,brs), 11.43(1H,s), 12.09(2H,brs).
6-21		2.31(3H,s), 3.91(2H,s), 7.23-7.27(2H,m), 7.34-7.53(6H,m), 7.80(1H,d,J=1.7Hz), 9.49(1H,brs), 9.86(1H,brs), 11.22(1H,brs), 11.81(1H,brs), 12.10(1H,s).

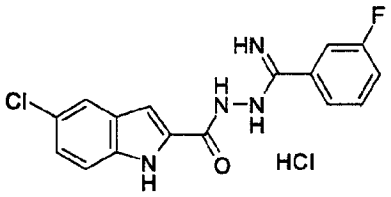
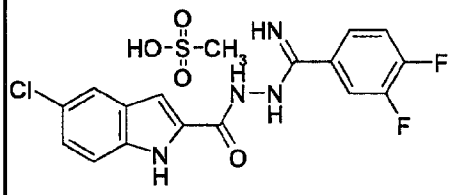
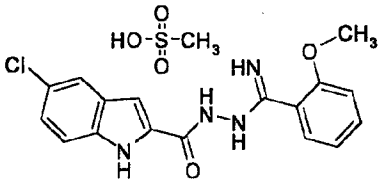
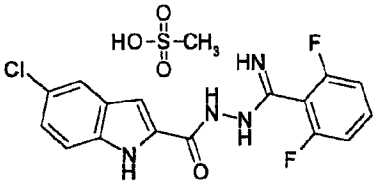
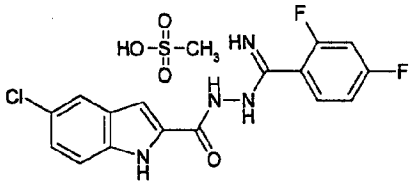
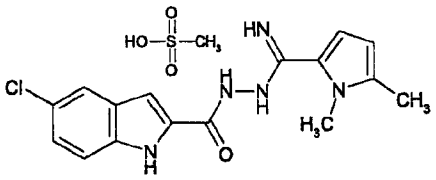
6-22		7.26(1H,dd,J=1.8,8.7Hz), 7.38(1H,s), 7.50,(1H,d,J=8.7Hz), 7.67-7.80(5H,m), 9.86(2H,brs), 11.54(1H,brs), 12.13(1H,s).
6-23		2.30(3H,s), 7.28(1H,dd,J=1.8,8.7Hz), 7.32(1H,s), 7.50(1H,d,J=8.7Hz), 7.79-7.85(3H,m), 8.04(1H,m), 9.94(2H,brs), 11.40(1H,brs), 12.09(1H,s).
6-24		2.29(3H,s), 3.91(3H,s), 7.18-7.34(4H,m), 7.50(1H,d,J=8.7Hz), 7.56(1H,d,J=7.5Hz), 7.71(1H,dd,J=7.5,8.7Hz), 7.81(1H,d,J=1.8Hz), 9.77(1H,brs), 9.85(1H,brs), 11.36(1H,brs), 11.64(1H,brs), 12.06(1H,s).

Table-34

Ex.	Structural formula	^{1}H-NMR(δ,300MHz,DMSO-d6)
6-25		2.30(3H,s), 7.27(1H,dd,J=1.7,8.7Hz), 7.30(1H,d,J=1.7Hz), 7.44-7.51(3H,m), 7.82,(1H,d,J=1.7Hz), 7.87(1H,m), 10.43(2H,brs), 11.51(1H,s), 12.11(1H,s).
6-26		2.30(3H,s), 7.27(1H,dd,J=2.0,8.8Hz), 7.30(1H,s), 7.45(1H,m), 7.50(1H,d,J=8.8Hz), 7.71(1H,m), 7.83(1H,s), 7.87(1H,m), 10.06(2H,brs), 11.44(1H,brs), 12.10(1H,brs), 12.10(1H,s).
6-27		2.30(3H,s), 2.34(3H,s), 3.71(3H,s), 6.14,(1H,d,J=4.1Hz), 6.84(1H,d,J=4.1Hz), 7.26,(1H,dd,J=2.2,8.9Hz), 7.29(1H,s), 7.50,(1H,d,J=8.9Hz), 7.81(1H,d,J=72.2Hz), 9.37(2H,brs), 11.23(2H,brs), 12.06(1H,s).

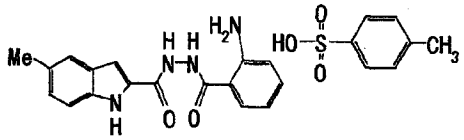
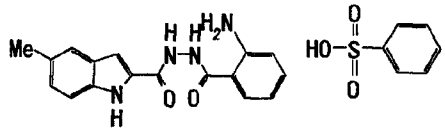
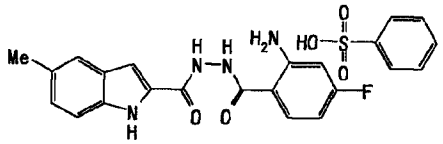
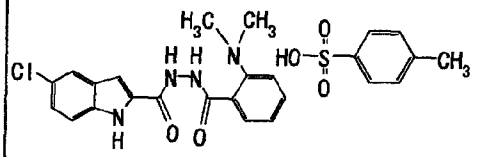
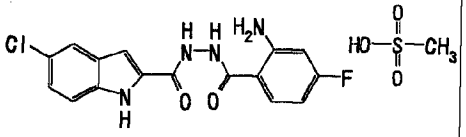
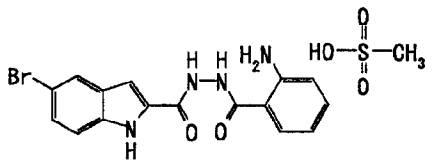
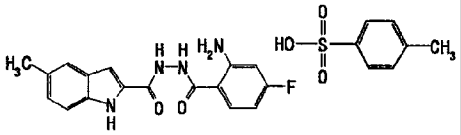
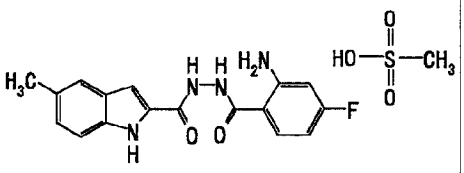
6-28		2.28(3H,s), 2.37(3H,s), 5.14(2H,m), 6.72(1H,m), 6.86(1H.m), 7.05(1H,d,J=8.4Hz), 7.12(2H,d,J=8.0Hz), 7.19(1H,s), 7.33(2H,m), 7.43(1H,s), 7.48(2H,d,J=7.4Hz), 7.67(1H,m), 10.24(1H,m), 10.37(1H,s), 11.56(1H,s).
6-29		2.38(3H,s), 4.56(2H,m), 6.69(1H,m), 6.83(1H,m), 7.05(1H,d,J=8.4Hz), 7.18(1H,s), 7.30-7.43(5H.m), 7.58-7.62(2H,m), 7.66(1H,m), 7.76(1H,d,J=1.8Hz), 10.24(1H,m), 10.36(1H,s), 11.58(1H,s).
6-30		2.38(3H,s), 5.89(2H,m), 6.39(1H,m), 6.52(1H,dd,J=11.2,2.6Hz), 7.04(1H,d,J=8.4Hz), 7.17(1H,s), 7.30-7.35(4H,m), 7.42(1H,s), 7.59-7.62(2H,m), 7.69(1H,m), 10.18(1H,brs), 10.33(1H,s), 11.57(1H,s).
6-31		2.29(3H,s), 3.06(6H,s), 7.11(2H,d,,J=7.8Hz), 7.21-7.28(2H,m) , 7.40-7.49,(4H,m), 7.66(2H,m), 7.30-7.36(4H,m), 7.78(1H,m), 7.87(1H,d,J=7.5Hz), 10.82(1H,s), 11.14(1H,s), 11.98(1H,s).
6-32		2.41(3H,s), 6.40(1H,dt,J=8.7,2.7Hz), 6.53(1H,dd,J=12.0,2.7Hz), 7.20-7.26,(2H.m), 7.46(1H,d,J=8.7Hz), 7.70,(1H,d,J=9.6,6.6Hz), 7.76(1H,d,J=1.8Hz), 10.24(1H,s), 10.50(1H,s), 11.94(1H,s).

Table-35

Ex.	Structural formula	^{1}H-NMR(δ,300MHz,DMSO-d6)
6-33		2.37(3H,s), 6.71(1H,m), 6.86(1H,d,J=8.2Hz) ,7.26-7.35(3H,m), 7.42(2H,d,J=8.7Hz), 7.68(1H,d,J=7.1Hz), 7.90(1H,d), 10.28(1H,brs), 10.51(1H,s), 11.93(1H,s).
6-34		2.29(3H,s), 2.38(3H,s), 6.39(1H,m), 6.52,(1H,dd,J=11.9,2.6Hz), 7.04(1H,d,J=7.1Hz), 7.11(2H,d,J=7.9Hz), 7.17(1H,s), 7.34(1H,d,J=8.4Hz), 7.42(1H,s), 7.48,(2H,d,J=8.1Hz), 7.69(1H,dd, J=8.8,6.6Hz), 10.17(1H,s), 10.32(1H,s), 11.56(1H,s).
6-35		2.38(3H,s), 6.38(1H,dt,J=8.6,2.6Hz), 6.52(1H,dd,J=11.9,2.6Hz), 7.04(1H,d,J=9.8Hz), 7.17(1H,s), 7.34(1H,d,J=8.4Hz), 7.42(1H,s), 7,69(1H,dd,J=8.8,6.7Hz), 10.17(1H,s), 10.32(1H,s), 11.56(1H,s).

Pharmacological Tests

Experimental Example (1) Measurement method of liver glycogen phosphorylase activity

The measurement of the glycogen phosphorylase activity was performed by measuring the concentration of phosphoric acic produced by a reverse reaction, that is, a reaction wherein the glycogen phosphorylase synthesizes glycogen from G1-P. A cell lysate of Sf9 cells that forcibly expressed recombinant human liver glycogen phosphorylase was diluted to a protein amount of 80 μg/mL with 1 mM imidazole-hydrochloric acid buffer (pH 7.0, containing 0.2 mM PMSF, 250 mM NaCl, 0.025% BSA) and the dilute cell lysate was used as an enzyme solution of human liver glycogen phosphorylase. As a substrate solution, 25 mM Tris-HCl buffer (pH 7.2, containing 250 mM KCl, 6.25 mM $MgCl_2$, 6.25 mM EGTA, 1.25 mM glucose-1-phosphate, 2.5 mg/ml glycogen, 7.5 mM glucose) was used. The test drug was dissolved in 0.5% dimethyl sulfoxide (DMSO). To a mixture of the test drug (10 μl) and the substrate solution (20 μl) was added an enzyme solution (20 μl) to start the enzyme reaction. As a control, 0.5% DMSO was added instead of the test drug. One free of addition of enzyme was used as a blank. The mixture was reacted at room temperature for 60 min, and a malachite green solution (50 μl) was added. The mixture was further reacted at room temperature for 20 min and absorbance at 650 nm was measured. An enzyme solution was added to the blank simultaneously with the malachite green solution and the measurement was done in the same manner. The percent inhibition (%) of the test drug was calculated from ((value of control - value of the test drug)/(value of control - value of blank))x100(%).

The test results of the above-mentioned Experimental Example are shown in Tables 36-38.

Table 36

Ex. No.	Enzyme inhibitory activity against HLGPa IC_{50} (μM)	Ex. No.	Enzyme inhibitory activity against HLGPa IC_{50} (μM)	Ex. No.	Enzyme inhibitory activity against HLGPa IC_{50} (μM)
1	0.038	1-36	>0.1	1-65	>0.1
1-2	0.013	1-37	>0.1	1-66	>0.1
1-3	0.037	1-38	>0.1	1-67	0.054
1-9	0.073	1-39	0.81	1-68	0.16
1-10	0.20	1-41	0.31	1-69	0.15
1-11	0.072	1-42	0.26	1-70	0.15
1-12	0.79	1-43	0.095	1-71	0.062
1-13	0.072	1-44	0.10	1-72	>0.1
1-14	0.13	1-46	0.29	1-73	0.076
1-15	0.12	1-47	0.66	1-75	0.25
1-16	0.073	1-49	0.15	1-76	0.037
1-18	0.099	1-50	0.027	1-78	0.018
1-19	0.091	1-51	0.089	1-79	0.083
1-20	0.035	1-52	0.091	1-80	0.40
1-21	0.049	1-53	0.23	1-81	0.028
1-23	0.075	1-54	0.030	1-82	0.36
1-24	0.17	1-55	0.087	1-83	0.88
1-25	0.14	1-57	0.030	1-84	0.02
1-26	0.018	1-58	>0.1	1-85	0.43
1-27	0.047	1-59	>0.1	1-86	0.028
1-28	0.049	1-60	>0.1	1-87	0.056
1-29	0.015	1-61	0.049	1-88	0.020
1-30	0.24	1-62	0.088	1-89	0.45
1-32	0.35	1-63	0.028	1-91	0.056
1-33	0.086	1-64	>0.1	1-92	0.071

Table 37

Ex. No.	Enzyme inhibitory activity against HLGPa IC_{50} (μM)	Ex. No.	Enzyme inhibitory activity against HLGPa IC_{50} (μM)	Ex. No.	Enzyme inhibitory activity against HLGPa IC_{50} (μM)
1-93	0.27	1-129	0.059	2-23	0.024
1-94	0.52	1-132	0.11	2-24	0.017
1-95	0.28	1-133	0.050	2-25	>0.1
1-97	0.010	1-134	0.040	2-26	0.21
1-98	0.087	1-136	0.27	2-27	0.30
1-99	0.010	1-137	0.33	2-28	0.056
1-100	0.24	1-138	0.46	2-29	0.27
1-101	0.035	1-139	0.38	2-30	0.088
1-102	>0.1	1-140	0.18	2-31	0.026
1-103	0.028	1-142	0.10	3	>0.1
1-104	0.021	1-143	0.12	3-3	0.078
1-105	0.087	2	0.016	3-5	0.19
1-106	0.078	2-2	0.071	3-6	0.19
1-107	0.054	2-9	>0.1	3-7	0.05
1-108	0.056	2-10	>0.1	3-8	0.10
1-109	0.14	2-11	>0.1	3-9	0.73
1-110	0.035	2-12	0.44	3-10	0.44
1-112	0.028	2-16	0.11	3-11	0.52
1-116	0.041	2-17	0.037	3-12	0.68
1-122	>0.1	2-18	0.040	3-13	0.44
1-123	>0.1	2-19	0.091	3-14	0.12
1-124	>0.1	2-20	0.022	3-15	0.15
1-125	0.19	2-21	>0.1	4	0.085
1-127	0.084	2-22	0.031	4-2	0.023
1-128	0.033				

Table 38

Ex. No.	Enzyme inhibitory activity against HLGPa IC_{50} (μM)	Ex. No.	Enzyme inhibitory activity against HLGPa IC_{50} (μM)	Ex. No.	Enzyme inhibitory activity against HLGPa IC_{50} (μM)
4-3	>0.1	4-20	0.17	6	0.062
4-4	>0.1	5-5	0.079	6-14	0.015
4-5	>0.1	5-6	0.049	6-15	0.059
4-6	0.065	5-7	0.088	6-16	0.059
4-7	>0.1	5-8	>0.1	6-17	0.080
4-8	>0.1	5-9	>0.1	6-18	0.049
4-9	>0.1	5-10	>0.1	6-19	0.053
4-10	>0.1	5-11	>0.1	6-20	0.11
4-11	>0.1	5-12	0.29	6-21	0.084
4-12	>0.1	5-13	0.41	6-23	0.067
4-13	>0.1	5-14	0.30	6-24	0.16
4-14	0.11	5-15	0.063	6-25	0.33
4-18	0.075	5-18	>0.1	6-27	0.17
4-19	0.096	5-19	0.36	6-28	0.25

Experimental Example (2) Measurement method of plasma glucose concentration

Using obesity type diabetes model db/db mice, the effect of the compound (1) of the present invention on glucose concentration in plasma was examined. The glucose concentration in the plasma of db/db mice (10-15 weeks of age) was measured, and the mice were grouped into 5 mice per group such that the average glucose concentration of plasma is leveled. After fasting for 4 hr, the test drug or a solvent (0.5% methyl cellulose) was orally administered to db/db mice, and plasma glucose concentration at 1 and 3 hr after the

administration was measured. The hypoglycemic effect of the test drug was evaluated by detecting a significant difference every hour between the solvent administration group and the test drug administration group (Dunnett's test).

The test results of the above-mentioned Experimental Example are shown in Table 39.

Table 39

Ex. No.	Minimum effective dose db/db mouse (mg/kg, p.o.)	Ex. No.	Minimum effective dose db/db mouse (mg/kg, p.o.)
1-2	10	4-16	10
1-81	10	4-19	10
1-88	10	6	3
1-134	10	6-15	3
2-17	10	6-16	3
2-23	3	6-17	3
2-24	3	6-18	3
3	10	6-19	3
4	10	6-20	3
4-6	10	6-21	10

Industrial Applicability

As is clear from the above-mentioned tests, the novel compound and a pharmaceutically acceptable salt thereof of the present invention strongly suppressed human liver glycogen phosphorylase. Because of the presence of such action mechanism, the compound (1) of the present invention is useful as a therapeutic agent for diabetes.

This application is based on a patent application No. 331501/2001 filed in Japan, the contents of which are hereby incorporated by reference.